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VECTOR SCORING SYSTEM FOR THE PRIORITIZATION OF ENVIRONMENTAL CONTAMINANTS

FINAL REPORT - PART I METHODOLOGY, RATIONALE & CRITERIA

Prepared by: CanTox Inc. and SENES Consultants Ltd.
and the Priority List Working Group,
Ontario Ministry of the Environment

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EXECUTIVE SUMMARY

There are many thousands of chemicals to which the Ontario environment may be exposed. It is not possible to simultaneously evaluate the impact of all of these chemicals. In order to develop a manageable list of chemicals with high priority for regulatory assessment, the Ontario Ministry of the Environment commissioned the development of the Vector Scoring System.

In this scoring system, chemicals are given numerical scores for various parameters (called vector elements) which describe their environmental behaviour, exposure potential and adverse effects on organisms in the environment, including humans. If no information can be found on a chemical, an asterisk is substituted for the score for that vector element. In addition, various element score modifiers can be applied under specific circumstances. For example, if the validity of the data available is questionable, a question mark is appended to the element score. If a worst-case value is used, the score is modified by appending an exclamation mark. The scores for the individual elements can be combined in specific ways to give a priority ranking for groups of chemicals. The methods of combining element scores can be adjusted to meet the needs of specific users of the scoring system.

The scoring system is divided into three phases. Each phase requires more specific information about a chemical than the previous phase. Chemicals are ranked in each phase and pass into the next phase according to their priority ranking. Phase 1 of the Vector Scoring System simply allows the Ministry of the Environment to determine which chemicals that may be present in the Ontario environment are actually considered in the scoring system (i.e., defines the input into the scoring system).

Phase 2 of the Vector Scoring System is made up of the following nine elements, divided into three broad groupings:

- a) Elements describing exposure ("E" elements):
 - P2E1 -Sources
 - P2E2 -Releases
 - P2E3 -Environmental Distribution
 - P2E4 -Environmental Transport
 - P2E5 -Environmental Persistence
 - P2E6 -Bioaccumulation
- b) Elements describing adverse effects ("T" elements):
 - P2E7 -Acute Lethality
 - P2E8 -Other Toxicity
- c) Element describing aesthetic Properties:
 - P2E9 -Undesirable Aesthetic Properties

Scores from zero to three are assigned for each element based on increasing severity of specific criteria. The criteria for Phase 2 elements rely heavily on chemical/physical properties and adverse effect indicators of chemicals that are readily available from summary-type data sources (i.e., books, review articles).

Once scores are generated for each element based on available information, the chemical is placed into a high, medium or low priority list, or lists indicating a lack of information or chemicals with undesirable aesthetic properties. Those chemicals on the high priority list enter phase 3 of the scoring system first, followed by those on the medium priority list. Those on the undesirable aesthetic properties list are automatic candidates for regulatory assessment in Phase 3.

Phase 3 of the scoring system is made up of the following fifteen elements in three broad categories:

a) Elements describing exposure parameters ("E" elements):

P3E1	-Environmental Concentrations - Air
P3E2	-Environmental Concentrations - Water
P3E3	-Environmental Concentrations - Soil
P3E4	-Environmental Concentrations - Sediment
P3E5	-Environmental Concentrations - Animals
P3E6	-Environmental Concentrations - Plants
P3E7	-Frequency of Dispersion

b) Elements describing adverse effects ("T" elements):

P3E8	-Acute Lethality
P3E9	-Sub-Lethal Effects on Non-mammalian Animals
P3E10	-Sub-Lethal Effects on Plants
P3E11	-Sub-Lethal Effects on Mammals
P3E12	-Teratogenicity
P3E13	-Genotoxicity/Mutagenicity
P3E14	-Carcinogenicity

c) Element describing undesirable properties

P3E15	-Undesirable Aesthetic Properties
-------	-----------------------------------

More effort and resources are needed to acquire information for this phase than for phase 2 (i.e., primary reference sources from a variety of databases provide the main information sources). Phase 3 element scores range from zero to ten. Once scores are generated, the chemical is placed on one of five lists: high, medium or low priority, inadequate information or undesirable aesthetic properties. Chemicals placed on the high priority list receive first assessment for regulatory consideration by the Ministry of Environment.

It is important to note that once vector scores are generated, they are recorded with the name of the chemical and can be used for visual ad hoc evaluation and for future reference. The Phase 3 element scores are combined using a specific set of combining rules in order to determine the list assignment, however, the scores for individual elements are never removed but accompany the chemical when it is placed on a list. This retention of information allows easy identification of problem areas or data gaps.

Structure-activity relationships and environmental modeling techniques can be used to estimate scores for vector elements in both Phases 2 and 3 where specific data are lacking. In such cases, the vector element scores should be modified with either a ? or !, depending on the particular circumstances involved. The procedures for use, and the limitations of using structure-activity relationships or environmental modeling techniques are outlined in appendices to the scoring system.

SOMMAIRE

L'environnement ontarien est exposé à des milliers de substances chimiques dont il est impossible d'évaluer l'incidence au cours d'une même étude. Toutefois, pour arriver à dresser une liste pratique des substances chimiques qu'il faut évaluer en priorité dans un but de réglementation, le ministère de l'Environnement de l'Ontario a demandé que soit conçu un système de notation vectoriel.

Ce système de notation permet d'attribuer aux substances chimiques, pour divers paramètres (appelés éléments vectoriels), une valeur numérique qui décrit le comportement des substances dans l'environnement, les risques d'exposition à ces substances et leurs effets néfastes sur les êtres vivants (y compris l'être humain). S'il est impossible de trouver des informations au sujet d'une substance, on remplace la valeur numérique de cet élément vectoriel par un astérisque. En outre, dans certaines circonstances, on peut appliquer un facteur modificateur à la valeur numérique attribuée. Par exemple, si la validité des données disponibles est douteuse, on adjoint à la valeur numérique un point d'interrogation. S'il s'agit d'une valeur correspondant au pire des cas, elle est modifiée par l'adjonction d'un point d'exclamation. On peut combiner les valeurs attribuées aux divers éléments vectoriels de façons particulières pour classer les substances chimiques par ordre de priorité. De plus, on peut utiliser diverses méthodes pour combiner les valeurs numériques en fonction des besoins des utilisateurs du système.

Le système de notation se divise en trois phases successives, chacune exigeant des informations plus précises que la phase précédente. Les substances sont classées à chaque phase et passent à la phase suivante selon leur ordre de priorité. Ainsi, la phase 1 du système de notation vectoriel permet tout au plus au ministère de l'Environnement de déterminer si une substance chimique pouvant se trouver dans l'environnement est incluse dans le système de notation vectoriel (en d'autres termes, elle détermine quels sont les paramètres du système).

La phase 2 se compose des neuf éléments suivants, répartis en trois grandes catégories :

- a) Éléments décrivant l'exposition (éléments "E") :
 - P2E1 - Sources
 - P2E2 - Émanations
 - P2E3 - Répartition dans l'environnement
 - P2E4 - Déplacement dans l'environnement
 - P2E5 - Persistance dans l'environnement
 - P2E6 - Bioaccumulation

- b) Éléments décrivant les effets néfastes (éléments "T") :
 - P2E7 - Létalité très élevée
 - P2E8 - Autre toxicité
- c) Éléments décrivant les propriétés esthétiques :
 - P2E9 - Propriétés esthétiques indésirables

Pour chaque vecteur, la substance évaluée reçoit une cote de zéro à trois selon l'accroissement de la gravité de critères donnés. Les critères des éléments de la phase 2 sont étroitement liés aux propriétés chimiques et physiques des substances et aux indicateurs d'effets néfastes que l'on trouve aisément dans les documents de synthèse (livres, articles spécialisés, etc.).

Une fois tous les éléments évalués à partir des données disponibles, la substance chimique est classée selon sa priorité (absolue, moyenne ou faible), ou placée sur une liste de substances pour lesquelles l'information est lacunaire ou encore, sur une liste de substances dont les propriétés esthétiques sont indésirables. Les substances de priorité absolue sont les premières à subir la phase 3 du système de notation, suivies des substances de priorité moyenne. Les produits chimiques figurant sur la liste des substances à propriétés esthétiques indésirables sont systématiquement soumis, à la phase 3, à l'évaluation en vue de la réglementation.

La phase 3 du système de notation se compose des quinze éléments suivants, répartis en trois grandes catégories :

- a) Éléments décrivant les paramètres relatifs à l'exposition (éléments "E") :
 - P3E1 - Concentrations dans l'environnement - Air
 - P3E2 - Concentrations dans l'environnement - Eau
 - P3E3 - Concentrations dans l'environnement - Sol
 - P3E4 - Concentrations dans l'environnement - Sédiments
 - P3E5 - Concentrations dans l'environnement - Faune
 - P3E6 - Concentrations dans l'environnement - Flore
 - P3E7 - Fréquence de la dispersion
- b) Éléments décrivant les effets néfastes (éléments "T") :
 - P3E8 - Létalité très élevée
 - P3E9 - Effets sublétaux sur les animaux autres que les mammifères
 - P3E10 - Effets sublétaux sur la flore
 - P3E11 - Effets sublétaux sur les mammifères
 - P3E12 - Pouvoir tératogène
 - P3E13 - Toxicité génétique ou pouvoir mutagène
 - P3E14 - Pouvoir Carcinogène

c) Éléments décrivant les propriétés indésirables
P3E15 - Propriétés esthétiques indésirables

La phase 3 exige encore plus de recherche et de ressources que la phase 2 (les principales sources d'information sont ici les sources de référence primordiales de diverses bases de données). La notation des éléments de la phase 3 va de zéro à dix. Une fois les diverses valeurs connues, la substance chimique est classée sur l'une des cinq listes suivantes : priorité absolue, priorité moyenne, faible priorité, renseignements incomplets ou propriétés esthétiques indésirables. Les substances chimiques figurant sur la liste de priorité absolue sont évaluées les premières par le ministère de l'Environnement de l'Ontario dans un but de réglementation.

Il importe de souligner qu'une fois attribuées, les notes vectorielles sont enregistrées avec le nom de la substance chimique à laquelle elles correspondent et qu'elles peuvent ensuite être utilisées au besoin pour simple consultation ou comme référence. On regroupe selon des règles précises les notes attribuées à la phase 3 afin de déterminer à quelles fonctions la liste sera affectée; toutefois, les notes attribuées à chacun des éléments ne sont jamais isolées; elles accompagnent le nom de la substance chimique chaque fois que cette dernière est ajoutée à une liste particulière. Cette façon de procéder permet de repérer aisément les domaines problématiques ou les données lacunaires.

Il est également possible de se servir des relations entre la structure et l'activité d'une substance ainsi que des techniques de modélisation pour estimer la valeur des éléments vectoriels des phases 2 et 3 lorsqu'on manque d'informations particulières. La valeur de l'élément vectoriel est alors modifiée par un "?" ou par un "!", selon les circonstances. Les modalités et les restrictions relatives à l'utilisation de ces modes d'évaluation sont exposées dans les annexes du système de notation.

1.0 INTRODUCTION

1.1 General Background

In November 1985, the team of CanTox Inc. and SENES Consultants Limited was engaged by the Ontario Ministry of the Environment (MOE) to provide scientific and technical expertise for the development, review, and testing of a methodology for assessing the potential environmental and health hazards of chemicals. The prime objective of the project was to provide the Hazardous Contaminants Coordination Branch of the MOE with a method for the identification and prioritization of chemicals as the initial step in the standard setting process.

The initial focal point for the project was provided by a Discussion Document developed by the Priority List Working Group (PLWG). The PLWG Discussion Document outlined a three-phase scoring system for the identification of the potential environmental and health hazards of chemicals. It was proposed that Phase 1 of the system would identify all of those substances that could be of concern to the MOE from the select universe of some 66,000 chemicals. Phase 2 would identify a subset of chemicals which require further, more detailed consideration by the MOE. Phase 3 would identify a final subset of chemicals from the Phase 2 subset that would be candidates for standard setting. Detailed environmental health hazard evaluations would be conducted on a high priority group from this final subset as part of the standard setting process. The scoring system (hereafter referred to as the "vector" scoring system) developed by the CanTox/SENES team, in conjunction with PLWG members, retained this three-phased format.

Advances in knowledge and improvements in the data available on chemicals will undoubtedly result in certain aspects of any scoring system becoming outdated. To remain effective, a scoring system must be flexible and lend itself to easy modification as new developments and information become available. The vector scoring system lends itself to review and updating.

1.2 Project Objectives

The methodology will allow the Hazardous Contaminants Coordination Branch to identify chemicals for which the development of multimedia standards is required, and will provide assessment criteria for the other Branches of the Ministry that are involved in the assessment of chemicals.

The efforts of the CanTox/SENES project team have focused primarily on Phases 2 and 3 of the PLWG document. Phase 1 was developed by the MOE. The overall project was divided into two parts:

- Part I consisted of the development of the scoring system based on the three phase approach of the PLWG document to provide a "state-of-the-art" method for the screening and prioritization of chemicals to identify those requiring detailed environmental and health assessment.
- Part II was an evaluation of the performance of the vector scoring system. This evaluation was based on a comparison of the reported potential environmental and health hazards of selected chemicals with the scores and levels of priority assigned to the selected chemicals by the vector system. The results of Part II forms a separate report.

2.0 THE VECTOR SCORING SYSTEM

2.1 Basic Principles and Philosophy

To effectively and efficiently use the limited resources available and remain responsive to concerns regarding substances in the environment, regulatory agencies often must assign priorities to the various issues they face to provide a guide to actions to be taken. Systems that assist in the ranking of substances are an outgrowth of the need to create priority lists. These systems provide a systematic approach for the identification of chemicals requiring more detailed assessment. In this way a screening or scoring system assists in the identification of potential hazards so appropriate corrective measures may be initiated before serious problems develop.

Scoring systems have been applied in a variety of ways to suit different user needs, ranging from identifying potentially dangerous food additives to ranking substances according to bio-accumulation potential. A system may take a quantitative approach such as using algorithms to combine or model data into a score or group of scores. Alternately, a qualitative approach may be used such as guidance through a series of questions (e.g. a decision tree) to give a relative ranking of a group of chemicals (e.g. low, moderate, high).

An approach commonly used in scoring systems is to translate the properties of a chemical into numerical scores so that different chemicals can be compared on a common basis. Several systems of this type are described in a comprehensive review of the different types of scoring systems developed and used by various groups around the world (Hushon and Kornreich, 1984). A brief summary of available systems is presented in Appendix A.

The scoring system described in this report is based on the use of vectors to describe the key properties or characteristics of chemicals. A vector consists of a number of elements. Each element represents a property or effect relevant to the assessment of the potential environmental and health hazards of a chemical. Scores are assigned to the various elements based on a strategy that increases in sophistication and complexity from Phase 1 through Phase 3. The magnitude of the score assigned to each element of the vector reflects the level of concern arising from that property or effects of the chemical.

In addition to the numerical value assigned to an element, various symbols are used to modify a score to indicate special concerns regarding the source of, or confidence in, the underlying data:

- If the data required are not available, an asterisk (*) is assigned to that vector element rather than a numerical score.

- If the data used are questionable (e.g. data from specific sites that may not represent conditions in Ontario, data lacking in documentation, data derived with outdated methods), a score is assigned to the element, but it is modified with a question mark (?) to indicate doubt regarding the confidence in the data.
- If the data used are perceived as representing a worst-case scenario (e.g. environmental concentration data from an accidental spill site, toxicity data from intravenous administration), the score for that element is modified with an exclamation mark (!).
- If the data used in the assignment of an element score are estimated from environmental modeling techniques or structure-activity relationships, the score for that element is modified with a superscript "e".

The evaluation of a chemical in this way generates a sequence of scores (one for each element) that reflects the information that helps characterize the potential hazard a chemical presents to the environment and health. This vector format provides a more comprehensive and meaningful representation of information than can be shown by single numerical values such as those generated by some other scoring systems (see Hushon and Kornreich, 1984).

2.2 Combining Element Scores

As noted in Section 1.1, the prime objective of this study was to develop a scoring system to meet the requirements of the Hazardous Contaminants Coordination Branch of the MOE. To meet that objective, a specific approach to combining and evaluating element scores was identified (as described in Chapters 5 and 7). Other potential users of the vector scoring system will have different objectives and requirements. Since the properties critical to assessing chemicals are summarized in the vector elements, the vector system has the flexibility to accommodate such differences simply by altering the ways in which element scores are combined. In some circumstances it is advantageous not to combine element scores, but rather to view the complete vector for a particular phase for groups of chemicals. This procedure allows the use of intuitive judgment in the selection of high priority chemicals.

The following discussion illustrates general ways in which element combining rules can be combined. A simple combining rule would add the scores of all of the elements of a vector and assign priorities to chemicals according to the magnitude of the sums. Such generalized summation of vector elements results in the loss of a great deal of information, with little, if any, gain in establishing priorities. Rather than assigning priorities based on total score, the combining rules described in

Chapters 5 and 7 assign chemicals to high, medium or low priority lists based on either relatively high scores in specific elements or combinations of scores in groups of selected elements.

Other combining rules determine the effects of various element score modifiers on the overall score of a chemical. For example, the presence of certain numbers of asterisks in defined groups of element modifies the list assignment for that chemical. This rule helps to keep the system sensitive to information gaps, yet not be driven by them. The effect of information gaps on chemical scoring systems is illustrated in a system developed by Mitre Corporation for the Federal Republic of Germany (Hushon et al., 1978). A relative priority ranking of 702 chemicals resulted in pesticides accounting for one-third of the 45 highest ranked chemicals. Since pesticides are all regulated substances, they tend to have comparatively complete data bases. Chemicals with inadequate data bases were generally assigned a lower priority ranking in the Mitre scoring system.

2.3 Information Sources

The determination of the adequacy of the information used in the development of scores for individual elements will undoubtedly involve some judgment. Less judgment, however, should be required in the development of element scores as one proceeds from Phase 1 through Phase 3.

In Phase 3, the data source requirements are more extensive and stringent, including sources such as authoritative reviews, study group reports and original research data (Table 8.3). The validity of data that have not been peer reviewed must be judged on an ad hoc basis. The requirement for peer review of data is not a strict requirement for the use of data in Phase 3 since the data used to judge the potential hazards posed by chemicals may be derived from proprietary information provided by industry. In most cases, such data will not have been peer reviewed and may be the only information available on a chemical. This information may be completely adequate and worthy of the highest confidence. Professional judgment is required to reach such conclusions.

2.4 General Nomenclature Used in the Vector Scoring Scheme

The convention used for identifying vector elements is as follows:

PaEb

where:

- a = scoring system phase (P) number (i.e., 1, 2 or 3), and
- b = number of the element (E) within the vector.

The convention used for identifying combining rules is as follows:

PaRc

where:

a = scoring system phase (P) number (i.e., 1, 2 or 3), and
c = the combining rule (R) number within the vector.

The convention used for identifying priority lists produced by combining elements is as follows:

PaLd

where:

a = scoring system phase (P) number (i.e., 1, 2 or 3), and
d = the chemical list (L) number.

3.0 PHASE 1

Phase 1 is the entry review stage of the scoring methodology. The input of chemicals into this phase is from the chemical lists advocated by recognized agencies or organizations that have regulatory and assessment responsibilities, specific chemicals of concern to the MOE, and chemical of concern to other government agencies, industry or the public that may be recommended for consideration. The mechanism for these inputs is currently under development. This listing procedures is similar to that developed by the MOE in 1982 (MOE, 1982).

The following lists of chemical will establish the initial P1L1:

- a) MOE's Chemicals for Further Evaluation
 - b) Substances for which MOE already has standards, guidelines, objectives, etc., for air, surface water, drinking water, soil, sediment, sewage, sewage sludge, waste, etc.
 - MOE, 1984. Water Management Goals, Policies, Objectives and Implementation Procedures of the Ministry of the Environment.
 - MOE, 1983. Ontario Drinking Water Objectives
 - MOE, 1986. List of Standards, Ambient Air Quality Criteria, Tentative Standards, Guidelines, and Provisional Guidelines for Air Contaminants. Ontario Reg. 308 under the Environmental Protection Act
 - MOE, 1986. Deviation of Significance of MOE "Upper Limits of Normal" Contaminants Guidelines. Air Resources Branch
 - MOE, 1985. Chemicals registered under the generator registration program. Regulation 309 under the Environmental Protection Act. General Waste Management
 - OMAF, 1978. Guidelines for Sewage Sludge Utilization on Agricultural Lands, Ontario Ministry of Agriculture and Food.
 - All pesticides scheduled for use in the Ontario Pesticides Act. Regulation 751.
- c) The IJC List of Contaminants found in the Great Lakes.
 - International Joint Commission, 1984. An inventory of Chemical Substances Identified in the Great Lakes. Great Lakes Water Quality Board.

d) Chemicals considered or under consideration by IARC and NTP (excluding negative carcinogens)

- International Agency for Research on Cancer. Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. World Health Organization.
- National Toxicology Program. Annual Report on Carcinogens. United States.

4.0 PHASE 2

4.1 Phase 2 Vector Elements

A basic objective in the development of Phase 2 was to select vector elements for which data are likely to be available or readily determined for individual chemicals, and that reliably indicate the potential environmental and health hazards.

The following nine elements in three generally classes are used in the Phase 2 vector:

Elements describing exposure ("E" elements):

- P2E1 - Sources
- P2E2 - Releases
- P2E3 - Environmental Distribution
- P2E4 - Environmental Transport
- P2E5 - Environmental Persistence
- P2E6 - Bioaccumulation

Elements describing adverse effects ("T" elements):

- P2E7 - Acute Lethality
- P2E8 - Other Toxicity

Element describing aesthetic Properties:

- P2E9 - Undesirable Aesthetic Properties

Generally, assessments of the toxicological and ecological effects of chemicals encompass the effects of the parent compound and its various breakdown products, except perhaps where transformation results from physical-chemical reactions unrelated to biological activity (e.g. photochemical degradation). If breakdown products are not considered in the process of evaluating the parent chemical, then they should be scored as individual chemicals.

The general rules described in Section 2.2 for using the element modifiers (e.g. asterisk, question mark, exclamation mark and superscript "e") apply to all the Phase 2 vector elements. A summary of the criteria for scoring the Phase 2 elements is presented in TABLE B-1, Appendix B.

4.1.1 Elements That Address Exposure Potential

The elements of this Phase 2 category describe, in general terms, the amounts of substances that might reach the environment or be found in the environment. These estimates are used as surrogates for exposure. Surrogates are used in an attempt to minimize searching for specific exposure data in Phase 2 since such data may be difficult to obtain or may not exist for many chemicals.

P2E1 Sources

Rationale

This element describes the amount of a substance that is produced, used, or imported in Ontario. Such information can serve as a general indicator of the amount potentially available for release to the environment and provides a broad indicator of the potential for exposure to the chemical (Hushon and Clerman, 1982). Information on sources has been used for similar purposes in other scoring systems (Konemann and Visser, 1983; Hushon and Kornreich, 1984).

The activities of production, usage (or consumption), and importation are collectively referred to as "sources" since each can act as a source of substances being released into the environment.

Scoring Criteria

Scores for this element are defined in terms of the amount produced, used, or imported in Ontario. The scoring criteria are based on proposed classifications recently developed by Environment Canada as part of the Inventory Requirements for Chemicals in Canadian Commerce (Smith, 1986).

ELEMENT SCORE	CRITERIA kg/year
3	⁴ >10
2	⁴ >300 to 10
1	>5 to 300
0	≤ 5

Suggested Information Sources

MOE Ontario Industrial Chemical Survey 1981 and updates -
Summarizes information on industrial chemicals used in Ontario.

CORPUS CPI Chemical Profiles -
Summarizes production and consumption data for industrial chemicals used in Canada.

TSCAPP database -
Summarizes data on the production of chemicals compiled for U.S. Toxic Substances Control Act Inventory.

P2E2 Releases

Rationale

This element indicates the relative amount of a substance that enters the Ontario environment. Two major causes of releases are losses that occur during production activities and losses that result from the ways substances are used. Releases can range from virtually all of some substances (e.g. certain pesticides) to effectively none for others (e.g. those used in totally closed systems).

Production activities are likely to be the main sources of releases for substances that are chemical intermediates, catalysts, or substances that are chemically converted during use. Releases during production occur largely via atmospheric emissions and liquid effluents, however, data concerning such releases are seldom available.

Various jurisdictions concerned with the environmental or health implications of specific chemicals [e.g. MOE, National Research Council Canada (NRCC), Health and Welfare Canada, the International Joint Commission on the Great Lakes (IJC), the International Agency for Research on Cancer (IARC)] have included estimates of losses to various regions (e.g. by province, nationally, to the Great Lakes Basin). The U.S. Environmental Protection Agency (EPA) and IARC also report typical release rates of chemicals according to general categories of industrial and commercial operations. These could be used to estimate production releases for Ontario if other data are not available. For example, the EPA has indicated that losses during production generally lie in the range of 0.1 to 8% of the production volume, with most less than 1% (Becker et al., 1979).

For some substances, the nature of their use may determine the extent of release to the environment. This includes chemicals that are applied directly to the environment such as pesticides, and those in consumer products (e.g. household cleaners, paints and adhesives). Consideration should also be given to whether or not a substance is chemically converted or destroyed during use. For example, greater than 90% of most fuels are converted to other substances during use.

The following release factors are based on the way(s) substances are used. They have been estimated for general classes of substances and expressed as percentages of production quantities (Rippen et al., 1985).

- Destructive uses (fuel, intermediates)	1-10%
- Contained uses (catalysts)	1-10%
- Open, non-destructive uses (cutting fluids)	10-100%
- Open dispersive uses (plasticizers)	100%
- Direct use in the environment (pesticides)	100%

Rippen et al. (1985) also proposed a method for estimating chemical uses and releases based solely on information about chemical structures. Such an approach could be used for scoring this element if more direct information is unavailable or as a check against a release rate estimated by other means. In addition, the release estimates by Rippen et al. (1985) may provide general guidelines for assigning scores to comparable classes of chemicals.

Other attempts have been made to estimate chemical release rates according to use patterns. For example, Rohleder et al. (1985) referred to a system that provides 37 classes of chemicals based on use patterns. Such information may assist in scoring chemicals according to the criteria outlined below.

Scoring Criteria

The scores for this element are proportional to the total amount of a chemical released to the environment. The amount is expressed as a percentage of the total produced or imported. Actual quantities released are not used, but can be calculated from the information in this element and P2E1.

Two sets of scoring criteria are provided. One is semi-quantitative in nature and more appropriate for chemicals where releases during production predominate. These criteria are similar to those developed for a system for setting priorities on chemicals in the Netherlands (Konemann and Visser, 1983). The second set of criteria are qualitative and based largely on product use. The nature of the available data will largely determine which set to use. If there is adequate information to use either set, that which results in the highest score should be used. Judgment is required if the sets of criteria generate different scores. In that event preference should be given to the score based on the better information.

ELEMENT SCORE	% Release ^a Estimation	CRITERIA Use Description
3	>30%	Use results in most of the substance being released directly to the environment OR used in an open, dispersive manner.
2	>3 - 30%	Use results in most of the substance being converted into other chemicals and the remainder released to the environment, OR largely stricted to industrial uses, OR very slowly released over time, OR shipped in large batches.
1	>0 - 3%	Use limited to closed or contained industrial systems such that there are no routine releases.
0	0%	Not used or imported in Ontario

^a At the time of manufacture or production.

Suggested Information Sources

U.S. EPA, 1977 and supplements -

Summarizes emission rates for various industrial activities.

MOE documents, including drinking water criteria reviews -

Often include data on Ontario manufacturers and estimates of environmental releases.

Becker et al., 1979 -

Provides emission rates for several industrial activities.

P2E3 Environmental Distribution

Rationale

This element describes the physical extent to which a substance is distributed in the Ontario environment. The area over which distribution occurs is assumed to be a surrogate for the total biomass that could be exposed to a substance. It also is assumed that the distribution of biomass is similar throughout the province, and therefore, distribution of a chemical over equal areas exposes comparable sized biomasses. The use of area, rather than other parameters such as numbers of persons exposed, gives equal consideration to all biological life forms.

Ideally, the area over which a substance is distributed is based upon measured environmental concentrations. If the points of release are relatively few and discrete, environmental dispersion models may also be used to estimate the extent of distribution. For many substances, however, such information will not likely be available or will be beyond the resources of a Phase 2 evaluation. Alternatively, environmental distribution can be inferred from the number of potential release sites in Ontario. Release sites also include producers and users, whether they be large industrial sites or individuals.

Scoring Criteria

There are two sets of descriptive criteria provided for this element. The first considers physical extent and frequency of detection or measurement. The second allows assignment of scores based on the number of release sites and their distribution across Ontario. If both sets of criteria can be used, the one that produces the higher score should be given preference, unless there is a much lower level of confidence associated with it.

For many substances, scoring this element will require considerable judgment and may be based on little more than an idea of use patterns of the substance.

ELEMENT SCORE	CRITERIA	
	Measurement Basis	OR Release Basis
3	Frequently measured over much of Ontario.	Many release sites located throughout Ontario.
2	Frequently measured but only at specific locations.	Relatively few release sites but not concentrated in a few locales.
1	Infrequently measured at specific locations.	Few release sites concentrated in a few locales.
0	Not yet detected in the Ontario environment.	No known release sites in Ontario.

Suggested Information Sources

MOE monitoring data -

Provide information on the concentrations of chemicals in the Ontario environment.

Environment Canada monitoring data -

Provide information on the concentrations of chemicals in environments of Ontario and elsewhere in Canada.

Health Protection Branch monitoring data -

Provide information on the concentrations of chemicals in foods.

EPA monitoring data -

Provide information on the concentrations of chemicals in the environment in the United States.

P2E4 Environmental Transport

Rationale

This element describes the transport of chemicals between environmental media. The environmental transport of a chemical is an important factor in evaluating its potential environmental and health hazards. Inter-media transport can be observed during field studies or by undertaking microcosm studies in a laboratory, but relatively few substances have been studied using such techniques. One way to estimate the environmental transport characteristics of a chemical is to use a simple mathematical model such as the Fugacity Level II model.

The Fugacity Level II model estimates the equilibrium distribution of a chemical released to the environment. The environmental media considered are air, water, soil and sediment. The model requires information about both the chemical and receiving environment. The necessary chemical properties are molecular weight, solubility, vapour pressure, and octanol-water partition coefficient. Approximate constants for key environmental processes or an estimate of overall environmental half-life are also needed. Each of the environmental media must be characterized. These characteristics are influenced by the size of the area being considered. Characteristics for southern Ontario are provided in Appendix D which also presents a general overview of the fugacity concept and models.

Environmental mobility can also be indicated by parameters such as solubility and vapour pressure. These parameters are widely reported in the literature and can be found with relative ease for most chemicals. The water solubilities of most common organic chemicals fall in the range of 1 to 10^5 g/m³ (Lyman *et al.*, 1982). Highly soluble substances are relatively mobile in surface and ground waters and tend to be more biodegradable than those with low solubility (Lyman *et al.*, 1982). The scores in this element are primarily a function of vapour pressure and solubility. These two properties are the major factors governing the potential migration of a chemical in the environment, and determining which receptors may be exposed for the various environmental pathways. Other elements in Phase 2 address persistence and other undesirable characteristics of the less soluble substances.

Vapour pressure is a measure of volatility and thus important in evaluating air exposure pathways. Vapour pressure of liquids range from 10^{-4} to 10^2 kPa and solids range down to 10^{-8} kPa (Lyman *et al.*, 1982). Vapour pressure can be estimated from other physical characteristics (for examples see Lyman *et al.*, 1982), but the collection of such information is beyond the scope of a Phase 2 assessment.

Scoring Criteria

The criteria for this element uses results from environmental models and/or individual parameter values. In addition, there are criteria for substances that are largely associated with fine particles (generally less than 10 μ m in size). Examples are fine particles associated with incinerator processes.

The scoring criteria for this element are as follows:

ELEMENT
SCORE

CRITERIA

- | | |
|---|---|
| 3 | <p>At least two media other than the receiving medium, each containing more than 20% of the chemical released;</p> <p style="text-align: center;">OR</p> <p>the vapour pressure is greater than 1 kPa and water solubility is greater than 100 g/m³;</p> <p style="text-align: center;">OR</p> <p>most of the chemical is associated with fine particles when released into the environment.</p> |
| 2 | <p>One or more media other than the receiving medium, each contain 10% to 20% of the chemical released;</p> <p style="text-align: center;">OR</p> <p>either the vapour pressure is greater than 1 kPa or water solubility is greater than 100 g/m³.</p> |
| 1 | <p>One or more media other than the receiving medium, each contain 5% to 10% of the chemical released;</p> <p style="text-align: center;">AND</p> <p>the vapour pressure is 1 kPa or less and water solubility is 100 g/m³ or less.</p> |
| 0 | <p>Less than 5% of the chemical released partitions into media other than the receiving medium;</p> <p style="text-align: center;">OR</p> <p>the vapour pressure is 1 kPa or less and water solubility is 100 g/m³ or less.</p> |

Factors for converting from different units than those used in the above criteria are:

1 mm Hg = 0.1333 kPa
 1 atmosphere = 101.3 kPa
 g/m³ = mg/L

Suggested Information Sources

Lyman *et al.*, 1982 -

A comprehensive reference of published values and estimation methods for various physical and chemical properties.

Verschuieren, 1983 -

A handbook of environmental data for organic chemicals.

ENVIROFATE and ISHOW databases -

Contain solubility, vapour pressure, partition coefficients for many chemicals.

ICF Inc., 1985 -

Contains tabulations of physical, chemical and environmental fate data for many organic substances and elements.

Mills et al., 1982 -

A compilation of physical, chemical and environmental fate data for many organic substances.

Mackay and Shiu, 1981 -

A compilation of physical and chemical parameters for organic substances.

Kenaga and Goring, 1980 -

A compilation of solubility, sorption and K_{ow} data.

Clayton and Clayton, 1981 -

A comprehensive reference of information on industrial chemicals.

Karickhoff, 1984 -

Discussion of sorption processes in general and K_{ow}/K_{oc} values in particular.

Amoore and Hautala, 1983 -

Information on volatilities of industrial chemicals.

Neely and Blau, 1985 -

Contains physical, chemical and fate data and estimation methods.

P2E5 Environmental Persistence

Rationale

This element describes the tendency for a chemical to persist in the environment. Substances in the environment can be subjected to a variety of processes including sorption, oxidation, hydrolysis, photodegradation and biodegradation. The net result of such processes may be expressed as the overall persistence of a substance in the environment. When quantified, persistence is usually expressed as the length of time required for one-half of the original amount of a substance to be degraded. It is analogous to parameters which may be presented as "rate of loss in natural systems", "overall half-life", or "50% recovery time". It is also similar to the "persistence" parameter calculated by fugacity models.

Half-lives of chemicals may vary from seconds to thousands of years (ICF Inc., 1985). Short half-lives generally indicate a lower level of concern. For example, environmental releases of substances with half-lives of less than a few days often will not result in significant accumulation in the environment. Conversely, those with half-lives of several months or longer can lead to substantial exposure or accumulation in the food chain.

Scoring Criteria

The criteria for this element are based on half-life values or on general descriptors of persistence. If scores can be assigned using both quantitative and qualitative criteria, the higher score should be used.

If half-life data are available, they will usually pertain to specific media as opposed to general environmental persistence. This information provides an indication of levels of concern regarding specific media. In such cases, it is recommended that the media providing the highest score be used.

If persistence values have not been reported and cannot be estimated by using environmental models, other types of information may offer guidance in developing a score for this element. For example, structure-activity relationships may provide general indications of persistence for relatively unknown substances structurally similar to more familiar substances. To assess the potential biodegradability of substances in waste-water treatment plants, test methods such as the static-culture-flask and shaker-flask techniques have been used (for example, see Tabak *et al.*, 1981). The results of these tests in general show good agreement with published work on biodegradability. Substances not degraded under test conditions cannot be presumed to be immune to microbial action in the environment. Accordingly, scores derived from SARs or biodegradability tests should be modified with a superscript "e", a question mark, or exclamation mark as appropriate.

ELEMENT
SCORE

CRITERIA

3	Half-life greater than 100 days; OR designated as very persistent.
2	Half-life of more than 50 but less than 100 days; OR designated as moderately persistent.
1	Half-life of more than 10 but less than 50 days; OR designated as slightly persistent.
0	Half-life of less than 10 days; OR designated as not persistent.

Suggested Information Sources

ICF Inc., 1985 -

Includes compilation of half-lives in several media for organic substances.

Mills et al., 1982 -

Includes compilation of half-lives in aquatic media for organic substances.

Verschuere, 1983 -

Includes half-lives and biodegradability test results for organic substances.

Publications of the Environmental Secretariat of the National Research Council of Canada Associate Committee on Scientific Criteria for Environmental Quality -

These publications include data on biodegradability for specific substances.

ENVIROFATE database -

Contains data on biodegradation rates for chemicals released to the environment.

Tabak et al., 1981 -

Includes results of biodegradability studies for more than 100 organic substances.

P2E6 Bioaccumulation

Rationale

This element describes the tendency for a substance to accumulate in biological systems. Three different terms are used in the literature to describe accumulation. Bioconcentration usually refers to the process of uptake from water; bioaccumulation to uptake from water and food, and biomagnification to uptake along food chains. None of these terms are precisely defined. In the current context, the term bioaccumulation is intended to convey the ability of a substance to accumulate in the tissues of organisms and is expressed in terms of a bioconcentration factor (BCF).

Most BCF values pertain to fish or other aquatic organisms and are calculated as the ratio of the concentration of a substance in the whole organism (or sometimes a specific tissue) on a wet weight basis to the concentration of the substance in the water at steady state (Veith et al., 1979). For organic substances, values of BCF range from about 1 to more than 1,000,000 (Lyman et al., 1982).

Bioaccumulation factors have also been determined for some terrestrial vertebrates but these data are less abundant and more difficult to locate than those for aquatic organisms. It is recommended for Phase 2 that data collection efforts first focus on BCF values for aquatic organisms.

The tendency of substances to bioaccumulate in tissue frequently has been related to hydrophobicity or lipophilicity (Veith et al., 1979). As a result, several regression equations have been suggested for predicting BCF values from octanol-water partition coefficient (K_{ow}) and other physico-chemical properties. Those that utilize K_{ow} values have been most widely investigated and are considered the most applicable (Neely et al., 1974; Veith et al., 1979; Lyman et al., 1982; Mackay, 1982; Geyer et al., 1985). Examples of these equations are:

$$\log BCF = 0.76 \log K_{ow} - 0.23 \text{ (Veith et al., 1979)}$$

or

$$BCF = 0.048 K_{ow} \text{ (Mackay, 1982)}$$

Several qualifications are necessary in the application of these equations for the estimation of BCFs:

- a) For substances with high K_{ow} values (e.g. $K_{ow} > 5.5$), the equations tend to overestimate the BCFs. It has been proposed that these effects relate to interference with the passage of such substances through biological membranes.

b) If the chemical ionizes, dissociates, chelates or sorbs strongly to dissolved or particulate organic matter, or other material, the estimated BCF is likely to be in error since the water concentration implied by the calculation is that of the truly dissolved material, not the total concentration.

c) If the chemical is readily metabolized, the observed BCFs will be lower than predicted.

d) There is evidence to suggest that for chemicals of high Kow in which food uptake is dominant, environmental BCFs may deviate from laboratory values.

Scoring Criteria

Scoring criteria for this element are defined in terms either BCF or log Kow. For this element, the qualifying factors related to high Kow values, dissociation, ionization, chelation, sorption, metabolism or predominance of food uptake have not been considered in the determination of scores. This should tend to produce somewhat higher scores than warranted for some organic substances. BCF values can be estimated only to within an order of magnitude using most of the correlations developed to date, and laboratory test situations are incapable of duplicating field situations (Lyman *et al.*, 1982). For example, the marked differences in BCFs between aquatic species are not considered and the general rule of operation would be to utilize the highest valid value reported.

If scores based on both the BCF and the Kow can be determined, preference should be given to the measured BCF values rather than those estimated based on Kow.

ELEMENT SCORE	BCF	CRITERIA log Kow
3	>15000	>6.0
2	>500 - 15000	>4.0 - 6.0
1	>20 - 500	>2.0 - 4.0
0	≤ 20	≤ 2.0

Suggested Information Sources:

- Lyman et al., 1982 -
Contains BCF and K_{ow} data and estimation methods.
- Geyer et al., 1984 -
Examines relationship between BCF and K_{ow}.
- Kenaga and Goring, 1980 -
Includes K_{ow} and BCF data for aquatic environments.
- Verschueren, 1983 -
Includes BCF and K_{ow} data for organic substances.
- Veith et al., 1979 -
Includes BCF and K_{ow} values.
- AQUIRE database -
Contains BCF data for aquatic organisms.
- Mackay, 1982 -
Examines correlations of BCFs.
- Garten and Trabalka, 1983 -
Contains BCF data for data for aquatic and terrestrial organisms.
- ICF Inc., 1985 -
Includes BCF data.
- Hansch and Leo, 1979 -
Describes how to estimate K_{ow} values.

4.1.2 Elements That Address Toxicity

P2E7 Acute Lethality

Rationale

This element describes the acute lethality of a chemical to biological systems. Short-term exposures to chemicals may produce acute toxic effects. The acute exposure levels required to produce lethal effects provide a general indicator of the acute toxic potential of a chemical. Acute lethality, usually measured within 1 to 7 days of exposure, may or may not provide indications of the effects of lower levels or longer durations of exposure to the chemical. The classifications of lethal effects are based on terminology commonly accepted in the literature on acute toxic effects of chemicals, namely LD50 values by oral or dermal exposure, or LC50 values by inhalation or aquatic exposure (EPA, 1975; Doull et al., 1980; Hayes, 1982; FDA, 1982).

Acute LD50 values are used because they provide a general indication of the toxicologic potential of a chemical and have historically been the initial type of data obtained when conducting a toxicological assessment of a chemical. Therefore, LD50 data are available for many chemicals. In the future, however, the initial toxicological assessments of chemicals will likely include data on acute tolerance rather than LD50 data. Acute tolerance studies involve observation (usually daily for 14 days) of groups of animals exposed to a range of dosages of a substance. Signs of toxicity, including lethality, are recorded and the exposure level which the animals can tolerate is estimated. Precise relationships between LD50s and acute tolerance values are not available. For the purposes of scoring substances in this element based on acute tolerance data, the LD50 or LC50 scores should be divided by 10.

Neither LD50 or acute tolerance values are precise measurements and values can vary substantially among species and between measurements on the same species. Therefore, judgment is required in the selection of LD50 and acute tolerance values for scoring chemicals. Data from all species (humans, laboratory animals, wildlife, vertebrates, invertebrates, etc.) may be used in scoring this element and values from the most sensitive species are preferred unless valid reasons indicate otherwise.

Route of exposure can substantially affect the estimates of acute lethality. For terrestrial animals, data from oral, dermal or inhalation exposures are preferred since these routes most closely resemble actual exposure conditions. In addition, data from dermal studies in which exposure was to the test material alone are preferable. Those dermal studies conducted using a vehicle (e.g. dimethylsulfoxide) may result in artificially high estimates of toxicity due to the facilitated transport of the test chemical through the skin.

Data from non-preferred routes of exposure (e.g. intravenous, intraperitoneal, subcutaneous, dermal with vehicle) may be used if no other data are available, however, scores developed from such data should be modified with either an exclamation mark (!) or question mark (?) as judged appropriate. Likewise, exposure routes for aquatic species other than by direct application to water should be modified as appropriate.

Criteria for phytotoxicity are not included in this element because of the difficulties in assessing lethality in plants. Non-lethal effects in both plants and animals are included in element P2E8, Other Toxicity.

Scoring Criteria

The scoring criteria for this element are comparable to those followed by the Transportation of Dangerous Goods Act (Transport Canada) and the State of Michigan Critical Materials Registry

(1986). The scoring criteria used are as follows:

ELEMENT SCORE	CRITERIA			
	ORAL LD50 mg/kg	DERMAL LD50 mg/kg	INHALATION LC50 mg/m ³	AQUATIC LC50 mg/L
3	<50	<50	<150	<10
2	50-500	50-500	150-1500	10-100
1	>500-5000	>500-5000	>1500-15000	>100-1000
0	>5000	>5000	>15000	>1000

Suggested Information Sources

AQUIRE database -

This database contains acute lethality values for aquatic and terrestrial species.

Brooke, L.T. et al., 1984-85 -

Acute toxicities of organic chemicals to fathead minnows (Pimephales promelas). Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, Superior, Wisconsin (2 volumes).

Hayes, 1982 -

Contains information on the toxicology of pesticides and associated chemicals with particular reference to effects in humans.

Ketchen et al., 1979 -

These Critical Material Data sheets contain information on the toxic potential of individual chemicals, including acute lethality data, in terrestrial species.

Merck Index -

The Merck Index lists indices of toxicity for many chemicals in terrestrial species.

Clayton and Clayton, 1981 -

Summarizes the toxic characteristics of a large number of industrial chemicals, primarily in terrestrial species.

RTECS database -

The Registry of Toxic Effects of Chemical Substances contains LD50 and LC50 values in a variety of terrestrial species, plus a limited amount of 96 hour LC50 values for aquatic species.

Verschueren, 1983 -

This information source lists chemical/physical properties of organic chemicals and their toxicity indices in terrestrial and aquatic species.

P2E8 Other Toxicity

Rationale

This element describes the properties of a chemical indicative of the non-lethal, adverse effects in animals or plants. Generally the effects considered are associated with multiple exposures to the chemical, however, non-lethal, acute effects are also included. Specific chronic effects (e.g. carcinogenicity, teratogenicity, mutagenicity), as considered in other scoring systems (see Hushon and Kornreich, 1984), are addressed in Phase 3. There will be a large number of chemicals, however, for which data on such effects will be unavailable or incomplete. This element is only intended to provide a means of signaling the potential for a chemical to produce effects other than acute lethality.

Scoring Criteria

Scoring criteria for this element are based on multiple exposures (i.e., greater than one). The adverse effects may be lethal or non-lethal. Ideally, chronic exposure should encompass a substantial portion of the life span of the test system. This is usually considered a minimum of one year in terrestrial animals (FDA, 1982), but may be as short as a few days in certain aquatic and plant test systems.

If adequate multiple exposure data are not available, element scores may be estimated from other types of data. In terrestrial animals, data from exposures of 90 days duration may provide reasonable estimates of longer term effects, although the validity of extrapolating such data to predict chronic effects is dependent on the characteristics of the chemical (biological half-life, lipid solubility, bioaccumulation potential, etc.) and the test system (FDA, 1982; Grice, 1984; Willes *et al.*, 1985). Consideration of these factors is even more critical when estimates of potential longer-term adverse effects are made by extrapolation of data from various short-term *in vivo* or *in vitro* test systems (Grice, 1984; Willes *et al.*, 1985). When long-term effects are estimated from short-term exposure data, the scores derived would require appropriate "flags" (e.g. (!), (?) or "e") determined by the judgment of the user.

Route of exposure is also important for adverse effects associated with multiple exposures following the same reasoning as outlined for element P2E8 (Acute Lethality). Data derived from studies where the test chemical was administered by non-preferred routes would also require appropriate "flags" at the judgment of the user.

Examples of the various end-points included as chronic effects are as follows:

- | | |
|-----------------------|---|
| Tumorigenicity | - Positive evidence of tumour development (malignant or benign) associated with exposure to the chemical. |
| Teratogenicity | - Positive evidence of developmental abnormalities detrimental to the survival, future development or well-being of the offspring associated with the exposure to the chemical. |
| Reproduction toxicity | - Adverse effects on reproduction as they affect the survival, development or well-being of the species, including interference with gonadal functions. |
| Genotoxicity | - Evidence in eukaryotic or prokaryotic organisms of DNA adduct formation, gene mutation, chromosomal effects (aberrations, sister chromatid exchange, etc.), DNA damage, neoplastic transformation, interference with DNA repair systems, etc. |
| General Toxicity | <p>- General depressions in body weight and body weight gains, general behavioral alterations in animal systems, changes in growth and yield of plants, alterations in plant reproduction, and increases in diseases secondary to chemical exposure.</p> <p>- Gross or microscopic alterations indicative of disease from toxic events.</p> <p>- Adverse or deleterious effects on organ systems or functions, alterations in secretions of exocrine and endocrine glands, alterations in the brain and peripheral nervous systems.</p> <p>- Biochemical effects.</p> |

If data are available on more than one of these effects, the effect occurring at the lowest exposure level in the most sensitive test system should be used in scoring. In addition, structure-activity relationships may provide estimates of the occurrence of chronic effects if data on the actual compound of is lacking (see Appendix C). Such estimates would be appropriately "flagged" with a ? or "e".

The scoring criteria are as follows:

ELEMENT SCORE	DESCRIPTIVE CRITERIA
3	Positive evidence of non-acutely lethal adverse effects in one or more species.
2	Positive evidence of non-acutely lethal adverse effects in some species and valid negative data in the same species (i.e., equivocal data).
1	Evidence of non-acutely lethal effects not necessarily detrimental to the continued survival, development or well-being of the test system (e.g. reversible biochemical effects).
0	No evidence of effects associated with chronic exposure based on adequate data in more than one species.

Suggested Information Sources

AQUIRE database -

This database contains some information on potential chronic effects of chemicals in aquatic and terrestrial species.

Hayes, 1982 -

Contains information on the toxicology of pesticides and associated chemicals with particular reference to effects in humans.

Ketchen et al., 1979 -

These Critical Material Data sheets contain information on the toxic potential of individual chemicals, including acute lethality data, in terrestrial species.

Merck Index -

Lists indices of toxicity for many chemicals in terrestrial species.

Clayton & Clayton 1981 -

Summarizes the toxic characteristics of a large number of industrial chemicals, primarily in terrestrial species.

RTECS database -

The Registry of Toxic Effects of Chemical Substances contains LD50 and LC50 values in a variety of terrestrial species, plus a limited amount of 96 hour LC50 values for aquatic species.

Soderman, 1983 -

Lists identified carcinogens and noncarcinogens and summarizes the genotoxicity data available on such chemicals. Up-dates of this reference would be valuable in scoring chemicals in Phase 2.

Verschueren, 1983 -

Lists chemical/physical properties of chemicals and their toxicity indices in terrestrial and aquatic species.

4.1.3 Element Addressing Undesirable Aesthetic Properties

P2E9 Undesirable Aesthetic Properties

Rationale

This element describes any properties of a chemical that are undesirable from an aesthetic point of view, independent of toxicological considerations. Certain chemicals have undesirable properties relevant to the public perception or sensory appreciation of the environment. These include substances that can adversely effect the appearance or palatability of water, form objectionable bottom deposits, foam, film, or scum, impart a disagreeable taste or odour to water or aquatic organisms (e.g. fish tainting), be visible in air or cause odours, or otherwise detract from the aesthetic appreciation of the environment.

Scoring Criteria

Two sets of criteria are used for scoring this element. The first is based on the concentrations in water at which undesirable aesthetic properties are realized. The second is based upon concentrations in air. If scores can be assigned for both sets, the criteria that produce the higher score should be given preference. The types of reported information that can be used to assign scores include taste thresholds, odour thresholds, concentrations at which tainting occurs, and concentrations at which changes in appearance become evident.

The criteria related to water effects are expressed in units of mg/L. Values reported in units of parts per million (ppm) can be used by assuming that 1 mg/L is approximately equivalent to 1 ppm. For air-related effects, such a simple conversion does not exist. Because much of the historical air data are reported in units of ppm, the criteria also use these units. Data reported in units such as mg/L or mg/m³ can be converted to ppm as follows:

$$[(\text{mg/L}) \times 24450] / \text{molecular weight} = \text{ppm}$$

$$\text{mg/m}^3 = [\text{ppm} \times \text{molecular weight} \times 0.92] / 22.4$$

ELEMENT SCORE	CRITERIA	
	Water Related Effects	Air Related Effects
3	Occur at <0.01 mg/L	Occur at <0.01 ppm
2	Occur at 0.01-10 mg/L	Occur at 0.01-10 ppm
1	Occur at >10 mg/L	Occur at >10 ppm
0	Not known to occur	Not known to occur

Suggested Information Sources

Verschueren, 1983 -

Includes taste and odour threshold for organic substances.

WHO, 1984 -

Includes aesthetic characteristics in its guidelines for drinking water quality.

Fazzalari, 1978 -

A compilation of odour and taste threshold data.

Amoore and Hautala, 1983 -

A comprehensive review of odour thresholds for industrial chemicals.

Two journals that frequently contain articles on taste and odour are the Journal of the Air Pollution Control Association and the Journal of the American Water Works Association.

5.0 COMBINING RULES FOR PHASE 2 ELEMENTS

5.1 General Considerations for Combining Rules

The elements of the vector scoring system describe the properties of chemicals important in assessing their potential adverse effects on the environment and health. Methods for using the Phase 2 vector for the selection of chemicals for consideration in Phase 3 depend on the specific requirements of the user. The combining rules proposed here are designed to address multi-media requirements such as those of the MOE.

For the purpose of simplifying the description of Phase 2 combining rules, the elements of the Phase 2 vector are discussed using the following groupings:

Exposure elements = P2E1 through P2E6 ("E" elements)

Toxicity elements = P2E7 and P2E8 ("T" elements)

Undesirable Aesthetic Properties element = P2E9

The following general principles are adopted in the combining rules for Phase 2:

- a) Rather than assigning a specific priority number to each chemical (i.e. one substance is number 4, another is number 25, etc.), chemicals are placed onto one of relatively few priority lists. The placement of a chemical on a list is determined by rules for combining scores (called combining rules). Those substances that generate the most concern, and for which there is sufficient information, are given the highest priority for consideration in Phase 3. For Phase 2, three lists are used, designating substances of high (P2L1), medium (P2L2) and low (P2L3) priority. In addition, a list is generated for chemicals with undesirable aesthetic properties (P2L4) and another for chemicals lacking sufficient information to enable scoring (P2L5).
- b) If asterisks (signifying inadequate information) prevent the assignment of scores for the "E" or "T" groups of elements, the chemical bypasses subsequent combining rules and is placed on an "inadequate information" list (P2L5). This rule assists in ensuring that chemicals within a list have roughly comparable data bases. Chemicals on list P2L5 could be used to prioritize information gathering. For example, chemicals lacking information for "E" elements but with high scores for "T" elements could receive high priority for gathering information required in the "E" elements. Similarly, chemicals lacking information for "T" elements but having information indicative of potentially high exposures could receive high priority for gather information on toxicological or ecological effects. To ensure chemicals

on P2L5 were not overlooked on completion of scoring a group of chemicals through Phase 3, chemicals on P2L5 could be combined with those on list P3L5 in Phase 3.

- c) When chemicals are assigned to priority lists, they are accompanied by all their vector elements including assigned scores and score-modifiers. This provides a "finger-print" for the chemical and ensures retention of all the information used in scoring. The element scores assist in sorting within lists and in the identification of factors critical to the prioritization of the chemical.

5.2 Specific Combining Rules for Phase 2

The combining rules for the elements of the Phase 2 vector are described below and presented as a flow-diagram in Figure 1. If a chemical meets the criteria of a combining rule, it enters the List number assigned by that rule. If it does not meet the criteria, it passes to the next combining rule.

P2R1 If the score for P2E9 (undesirable aesthetic properties) is greater than or equal to 1, place the chemical on P2L4, then pass it to P2R2. If this criterion is not met, the chemical is also passed to P2R2.

P2R1 ensures that chemicals with undesirable aesthetic properties are identified. Chemicals on list P2L4 are compared with lists produced at the end of Phase 3 to identify chemicals with undesirable aesthetic properties that are not considered for regulation based on other criteria. Certain aesthetic properties may be critical enough to require regulation of a chemical even though it may not have significant environmental or health hazards.

P2R2 If the scores for either P2E7 (acute lethality) or P2E8 (other toxicities) are equal to 3, regardless of the scores for other elements, place the chemical on P2L1. If not, pass the chemical to P2R3.

This combining rule ensures that highly toxic chemicals receive due consideration for Phase 3 assessment. Such chemicals may be of high concern, even if scores for other elements are low.

P2R3 If elements in groups "E" or "T" contain sufficient numbers of asterisks (*) to prevent the combining of scores, place the chemical on P2L5. If not, pass the chemical to P2R4. Scores cannot be combined unless there are two group "E" elements and one group "T" element with scores.

P2R3 is designed to identify chemicals with insufficient data for a realistic assessment and which, because of missing information, may not be compared on an equivalent basis with other chemicals. List P2L5 will be added as a sub-set (including all vector element scores) to a comparable list from Phase 3 to group chemicals with insufficient information for scoring and identify potential candidates for further study.

- P2R4 If the sum of the maximum scores of two elements in the "E" group and one element in the "T" group is greater than or equal to 4, and the toxicity group is not zero, enter the chemical on P2L2. If not, pass the chemical to P2L3. This combining rule assigns low priority (P2L3) to chemicals with low toxicity and low exposure potential.
- P2R5 If the sum of the maximum scores of two elements in the exposure group and one element in the toxicity group for the chemicals on P2L2 are greater an or equal to 6, and the neither the "E" nor "T" groups are zero, place the chemical in P2L1. If not, leave the chemical on P2L2.

5.3 Selection of Chemicals for Phase 3

The entry of chemicals into Phase 3 is based on the following steps:

- a) Chemicals from P2L1 receive highest priority for entry into Phase 3. P2L1 contains chemicals with high levels of toxicity (e.g. scores of 3 in the toxicity elements) or moderate toxicity and high exposure potential. Highly toxic chemicals appear on P2L1 even though they may have scores of zero (0) or numbers of asterisks (*) that prevent combining of scores. The impact of such information is assessed in the more detailed criteria in Phase 3.
- b) Chemicals on P2L2 are assigned moderate priority and would enter Phase 3 following those from P2L1.
- c) Chemicals on P2L3 are assigned the lowest priority and likely would not enter Phase 3. If, however, judgment based on a visual assessment of the vector finger print indicated a potential problem chemical, it could be passed to Phase 3.
- d) Within-list sorting can be performed to determine which chemicals from P2L1 should be considered first in Phase 3. Since the characteristics of both exposure and toxicity determine potential hazard, the highest priority chemicals from P2L1 should be those with high toxicity and high

exposure potential. The system for within list sorting is based on the sum of the element scores. No information is lost in this process since the "finger-print" of element scores are retained with each chemical.

There are, however, 3 times as many "E" group as "T" group elements, therefore, the "E" elements are weighted and the elements are summed according to the following formula:

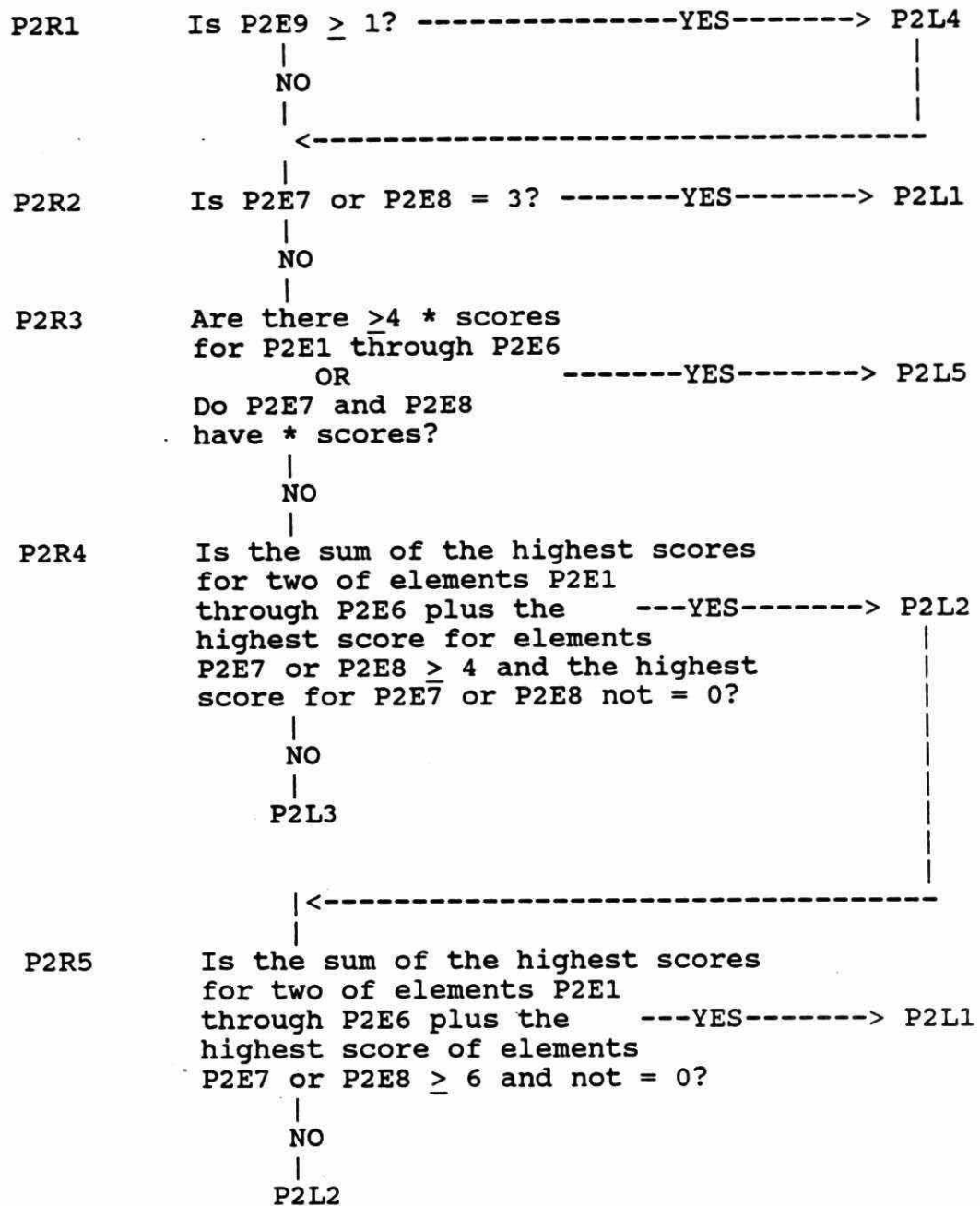
Element Sum = "E"/3 + "T", where

"E"/3 = (sum of "E" group elements)/3, and
 "T" = sum of "T" group elements.

In summing element scores, treat asterisks as 0. Considerable judgment must be exercised in conducting within list prioritization. The impact of element score modifiers (e.g. *, !, ? or e) on the prioritization of chemicals should be assessed on an ad hoc basis after the element sums for chemicals in P2L1 have been calculated. This assessment will help reduce the impact of compounding worst-case data estimates or questionable data on the final selection of a chemical for Phase 3.

Chemicals that pose potential hazards to the environment and health, but lack information critical to their prioritization, would be identified by ad hoc examination of the Phase 2 vectors of chemicals from P2L1 and P2L5. The selected chemicals would be placed on a "priority-information" list identifying those chemicals for which data should be gathered for elements critical to the completion of their Phase 2 scoring. This system should prevent "over-loading" of Phase 3 by ensuring that only chemicals with a certain minimum information base enter Phase 3.

FIGURE 1 Flow Diagram for Phase 2 Combining Rules



6.0 PHASE 3

The basic approach for Phase 3 of the vector scoring system is similar to Phase 2. However, the Phase 3 vector has a greater number of elements and the assignment of element scores requires more detailed information about the chemical. The Phase 3 elements describe those properties critical to determining the need for the regulation of a chemical.

Phase 3 of the vector system requires less detailed information than needed for the complete regulatory process, so that the scoring of large numbers of chemicals can be accomplished as quickly as possible. A balance is required, however, in the level of detail needed in the scoring system in order to minimize the possibility of the elimination of potentially hazardous chemicals from further consideration. To minimize this possibility, the Phase 3 criteria tend to be conservative in nature.

The 15 elements of the Phase 3 vector are listed below. A summary of the criteria for the assignment of scores to the elements is presented in Table B-2, Appendix B.

Elements describing exposure parameters ("E" elements):

P3E1	Environmental Concentrations - Air
P3E2	Environmental Concentrations - Water
P3E3	Environmental Concentrations - Soil
P3E4	Environmental Concentrations - Sediment
P3E5	Environmental Concentrations - Animals
P3E6	Environmental Concentrations - Plants
P3E7	Frequency of Dispersion

Elements describing adverse effects ("T" elements):

P3E8	Acute Lethality
P3E9	Sub-Lethal Effects on Non-mammalian Animals
P3E10	Sub-Lethal Effects on Plants
P3E11	Sub-Lethal Effects on Mammals
P3E12	Teratogenicity
P3E13	Genotoxicity/Mutagenicity
P3E14	Carcinogenicity

Element describing undesirable properties

P3E15	Undesirable Aesthetic Properties
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As with the Phase 2 of the screening system, modifiers can be applied to the scores of the vector elements as appropriate (e.g. * = no information; ? = questionable information; ! = worst-case information; e = score estimated using environmental modeling techniques or structure-activity relationships).

Elements were selected for the Phase 3 vector based on the premise that the potential hazards to the environment and health from a chemical depend on the level of exposure to the chemical and its toxicological characteristics. It was assumed that the exposure potential is proportional to the concentrations of the chemical in various environmental compartments. The U.S. Office of Science and Technology Policy (OSTP, 1985) concluded that there is no single procedure applicable to a complete assessment of exposure to chemicals. Consequently, exposure assessments are usually conducted on a case-by-case basis, integrating information from all potential exposure routes through all media utilizing measured environmental concentrations and/or outputs from models of environmental behaviour. Ideally, such an assessment generates a range of exposure values based on concentrations in different environmental compartments (OSTP, 1985). This philosophy formed the basis for the selection of the elements describing environmental concentrations and frequency of exposure in the Phase 3 vector (P3E1 to P3E7).

The elements describing toxicological characteristics (P3E8 to P3E14) focus on indicators of critical adverse effects of chemicals on all species of plants and animals in the environment. In the case of plant and animal populations, data are usually available for specific species but adequate data are seldom available on humans per se. Therefore, the majority of the criteria used in the development of scores for the elements describing the toxicology of a chemical are based on data from species other than humans. Adequate data on toxicity in other species are generally accepted by a variety of regulatory agencies as applicable to humans (FDA, 1982; IARC, 1983; OSTP, 1985; Willes et al., 1985). The difficulties inherent in the extrapolation of data among species may be addressed more carefully during the detailed regulatory evaluation of high priority chemicals selected from Phase 3.

The undesirable aesthetic properties identified in Phase 2, element P2E8 are carried forward to Phase 3 (element P3E15). This ensures that such properties are identified as part of the Phase 3 vector.

6.1 Elements Describing Environmental Concentrations

Elements P3E1 through P3E6 describe the concentrations of chemicals in six specific compartments of the environment: air, water, soil, sediment, animals (terrestrial and aquatic) and plants.

Measured concentrations of the chemical in the Ontario environment are the preferred data for scoring these elements. For many chemicals, however, measured concentrations will not be available. In such circumstances, or where data are perceived to be unreliable or unsuitable, modeling techniques can be used to estimate environmental concentrations. Several models are

available with differing capabilities for estimating such concentrations. A group of models based on the concept of fugacity are recommended for use in this scoring system. A brief description of the salient features of fugacity models are provided in Appendix D.

Most models, including the fugacity models, cannot estimate the concentrations of all chemicals in all environmental compartments. Procedures for estimating concentrations of chemicals in soil/sediment, plants and animals using models must be considered preliminary. Predicting the concentrations of inorganic substances in environmental compartments is in the developmental phase. Research and development into modeling techniques continues in many forms and as improvements evolve they should be incorporated into the scoring system.

The approach recommended for this scoring system is to use measured concentrations of chemicals in Ontario where data are available, and also use the model to gain experience in its use, applicability and validity. Such a comparative data base will prove invaluable in assessing chemicals for which no environmental concentrations have been measured.

The concentration in each of the six compartments is assessed by conversion of the various analytical units of measurement (e.g. mg/L, ug/m³) into a series of scales or scores on a logarithmic basis according to the following general relationship:

$$\text{Element Score} = A \log (\text{concentration}) + B,$$

where A and B are constants for each element. The score/concentrations are given later in tabular form for convenience.

Data from other locations similar to Ontario may also be used in scoring, but the resultant scores may require appropriate modifiers (e.g. ?, !) depending on the judgment of the scorer. Likewise, whenever models are used to estimate concentrations, the resulting scores for these elements should be modified with "e" to indicate that the scores are based on estimated concentrations.

The general scoring criteria for these elements are based on a standardized or normalized exposure potential for all compartments. The same score is assigned for all six elements if the concentration of the chemical results in a comparable level of intake from all compartments for a given receptor. The assignment of scores in such a manner requires the standardization of several characteristics of the exposed receptor. Man was chosen as the receptor for the normalization of exposure data. Humans were chosen because their exposure is of major concern and a well-developed data base exists which describes various exposure parameters in humans. Any other

environmental receptor for which adequate data exists could be used to normalize concentrations among environmental compartments and the overall results should be similar.

The receptor was assumed to weigh 60 kg, a weight mid-way between that routinely used to represent adult males (70 kg) and adult females (50 to 55 kg). The receptor was also assigned intake rates of 20 m³/day of air (ICF, 1985), 2 litres/day of water (NAS, 1977), 1.0 kg/day of plant produce and 1.0 kg/day of animal produce (Nutrition Canada, 1977). These exposure parameters are discussed in detail in the description of the appropriate elements.

The relationship between concentration and exposure was established such that exposures of 100 ug of chemical/kg body weight/day or more would receive the highest score of 10, and the scores would decline with exposure as follows:

ELEMENT SCORE	EXPOSURE (ug/kg/day)
10	>100
8	>10 to 100
6	>1 to 10
4	>0.1 to 1
2	≥0.01 to 0.1
0	no exposure

The daily exposure value used to normalize the highest concentration score was chosen based on historical information regarding those concentrations of chemicals generally perceived to be of some environmental concern. The values used were intended only to normalize concentrations in environmental compartments. They were not intended to encompass a complete range of intakes as related to specific toxicological end-points for humans or any other receptor. Neither was any relationship to a virtually safe dose, an acceptable daily intake, or a no-observable-adverse-effects-level intended. Rather, the relationship was designed to present a general appreciation of the potential exposure to a chemical and provide a common base for the comparison of concentrations in different environmental compartments.

Preference has been given to different sources of estimates of the concentrations of chemicals in the various environmental compartments according to the following guidelines:

a) Concentrations Measured in Ontario

Prior to score assignment, information regarding concentrations measured in Ontario should be gathered and summarized. Such information may be evaluated vis-a-vis the sources of the data, the size of the areas over which exposures could occur, and the frequency at which

various concentrations have been measured. Useful summary data include monitoring locations, dates, maximum, minimum, and mean values, detection limits, and indications of the distributions of results (e.g. the percentage of measurements below the detection limit or the presence of outliers that skew a distribution). Whether such information is abundant or sparse, judgment is required to determine the appropriate concentrations to use in scoring.

b) Estimated Concentrations Using Modeling Techniques

Even when Ontario data are available, concentrations of chemicals in the various environmental compartments should be estimated using models. These models use emission data, physical/chemical properties and persistence estimates. Element scores developed using environmental modeling techniques are modified with an "e".

c) Estimated Concentrations Using Data From Outside Ontario

If Ontario data are not available, data from other locations can also be used. These data may be used in combination with modeling techniques. The relevancy of data from other locations to conditions in Ontario will need evaluation. If such relevance is questionable, the element scores developed require a "?" modifier.

P3E1 Environmental Concentrations - Air

Rationale

This element describes the concentrations of a substance in Ontario air. Assessment of potential exposures of all organisms in the environment to a chemical requires knowledge of the concentration and distribution of a chemical in the atmosphere (Hushon and Kornreich, 1984). The atmosphere also provides a major route for the dispersion of chemicals into other compartments of the environment.

Air concentrations of chemicals may be estimated using environmental modeling techniques, such as the fugacity model, or from structure-activity relationships (particularly for different species of the same chemical) if monitoring data are unavailable.

Scoring Criteria

As outlined in the general rationale, the air concentration scoring criteria are normalized relative to human exposure. An average 60 kg individual is assumed to respire 20 m³ of air per day. Therefore, an air concentration of 300 ug/m³ [(100 ug/kg X 60 kg)/20 m³] or more results in an assigned score of ten. The element score decreases by two for each ten-fold decrease in the air concentrations.

The concentrations in air are derived from (in order of preference), a) concentrations measured in Ontario; b) concentrations estimated using environmental modeling techniques; or c) data from outside Ontario. Even for data gathered in Ontario, measurements of air concentrations may have been taken near major sources, so that they may not be representative of larger areas. Modeling techniques may be used to estimate average concentrations over wide areas. Scorer judgment is needed to evaluate the relevance of the available data to Ontario generally. Information from these sources is then used to assign scores as follows:

ELEMENT SCORE	AIR CONCENTRATION or DETECTION LIMIT (ug/m ³)
10	>300
8	>30 to 300
6	>3 to 30
4	>0.3 to 3
2	≥0.03 to 0.3
0	<0.03

Suggested Information Sources

Information regarding concentrations of atmospheric chemicals is available from air quality monitoring studies from the MOE, Environment Canada, U.S. Environmental Protection Agency, World Health Organization, and OECD.

P3E2 Environmental Concentrations - Water

Rationale

This element describes the concentrations of a chemical in water in Ontario. The estimation of exposures of aquatic species, various forms of wildlife and of human populations requires knowledge of the concentrations of chemicals in surface water. Chemicals in surface water can also influence exposure through other media by dispersion to other environmental compartments (e.g. soils/sediments, plants, aquatic and terrestrial animals, etc.). Environmental modeling techniques may be used to estimate water concentrations where monitoring data are lacking or inadequate.

Scoring Criteria

As outlined in the general rationale, the scoring criteria for water concentrations are normalized relative to human exposure. The criteria used assume an average 60 kg individual consuming two litres of water per day. Therefore, water concentrations of 3000 ug/L $[(100 \text{ ug/kg} \times 60 \text{ kg})/2 \text{ L}]$ or more are assigned a score of ten. The element score decreases by two for each ten-fold decrease in water concentrations.

The concentrations of chemicals in water are determined from (in order of preference), a) concentrations measured in Ontario; b) concentrations estimated using environmental modeling techniques; or c) data from outside Ontario. Even for data gathered in Ontario, most measurements of water concentrations have been taken near input sources, so that they may not be representative of larger areas. Modeling techniques may be used to estimate average concentrations over wide areas. Appropriate score modifiers should be used as required. Information from these sources are then used to assign scores as follows:

ELEMENT SCORE	WATER CONCENTRATION or DETECTION LIMIT (ug/m ³)
10	>3000
8	>300 to 3000
6	>30 to 300
4	>3 to 30
2	≥0.3 to 3
0	<0.3

Suggested Information Sources

Information regarding the concentrations of chemicals in water is available from water quality monitoring studies from the MOE "Water Quality Data" annual reports and reports for specific Ontario drainage basins, IJC Great Lakes Water Quality Board reports, reports from the Inland Waters Directorate of Environment Canada and the U.S. EPA Ambient Water Quality Criteria Documents.

P3E3 Environmental Concentrations - Soil

Rationale

This element describes the concentrations of a chemical in soil in Ontario. The assessment of the potential exposure of various terrestrial plants (including fruits and vegetables), and the general distribution of the chemical in the environment requires information regarding the concentrations of chemicals in soil.

Scoring Criteria

The scoring criteria for soil are based on the relationship between levels of chemicals in plants and those in soils. These relationships have been studied for some chemical substances, notably several pesticides and a few persistent aromatic hydrocarbons, but relatively little has been published about the uptake by plants of most organic chemicals in soils. The major mechanisms of uptake by plants are through the root system (which is probably relatively more important for highly soluble substances and for root crops) and by deposition on leaves (which may be more important for more volatile chemicals and leafy plants).

Many factors influence plant uptake of a chemical. These include the chemical properties of a substance, type of plant, length of growing season, soil characteristics, crop yield, and run-off by precipitation (Edwards, 1983; Hetrick and McDowell-Boyer, 1984). Based on the relatively limited number of observations reported in the literature, the ratio of concentrations in plants to soils range from approximately 1:1 to 1×10^{-4} :1 on a dry weight basis (i.e. levels in plants are generally lower than those in soil). Chemical concentrations in plants expressed on a dry weight basis are typically divided by a factor of five to estimate levels on a wet weight basis.

Much of the data suggest that uptake of organic chemicals by plant root systems is inversely proportional to the Koc and/or Kow values of the chemical and equations have been developed to predict plant uptake based on those properties (for example Carsel *et al.*, 1984). Based on this apparent correlation, the following simple relationship between Kow and plant uptake (based on wet weight basis) is used for relating the concentrations of chemicals in soils to concentrations in plants:

log Kow	Plant Uptake Factor
<1	1.0
>1 to 3	0.1
>3 to 5	0.01
>5	0.001

This relationship does not use Koc values, but if they are available and the organic carbon content of the soil is available or estimated, then Kow values may be derived (see Lyman et al., 1982).

These uptake factors are used to assign scores for different soil concentrations of a chemical in the following manner: Assuming a 60 kg individual consumes 1 kg of plant produce daily (see element P3E5), a chemical with a Kow ≤ 1 would be assigned a score of 10 if its soil concentration is 6000 ug/kg ($100 \text{ ug/kg/d} \times 60 \text{ kg} / (1 \text{ kg/d} \times 1.0)$) or more. For chemicals with Kow values greater than 1, the soil concentrations required for the assignment of a score of 10 would increase proportionally to the uptake factor to a value of 6,000,000 ug/kg (6g/kg) when the Kow is greater than 5.

The information on the concentrations of chemicals in soil is derived from (in order of preference), a) concentrations measured in Ontario; b) concentrations estimated using environmental modeling techniques; or c) data from outside Ontario. Even for data gathered in Ontario, most measurements of soil concentrations have been collected from areas near major sources, so that they may not be representative of larger areas. Modeling techniques could be used to estimate average concentrations over wide areas.

Information from these sources are then used in the assignment of scores for this element as follows:

SOIL CONCENTRATION or DETECTION LIMIT (ug/kg)

ELEMENT SCORE	K _{ow} <1	K _{ow} 1-3	K _{ow} 3-5	K _{ow} >5
10	$>6 \times 10^3$	$>6 \times 10^4$	$>6 \times 10^5$	$>6 \times 10^6$
8	$>6 \times 10^2 - 6 \times 10^3$	$>6 \times 10^3 - 6 \times 10^4$	$>6 \times 10^4 - 6 \times 10^5$	$>6 \times 10^5 - 6 \times 10^6$
6	$>60 - 6 \times 10^2$	$>6 \times 10^2 - 6 \times 10^3$	$>6 \times 10^3 - 6 \times 10^4$	$>6 \times 10^4 - 6 \times 10^5$
4	$>6 - 60$	$>60 - 6 \times 10^1$	$>6 \times 10^2 - 6 \times 10^3$	$>6 \times 10^3 - 6 \times 10^4$
2	$\geq 6 \times 10^{-1} - 6$	$\geq 6 - 60$	$\geq 60 - 6 \times 10^2$	$\geq 6 \times 10^2 - 6 \times 10^3$
0	$< 6 \times 10^{-1}$	< 6	< 60	< 600

Suggested Information Sources

Information regarding the concentrations of chemicals in soils is available from soil monitoring studies from the MOE. In addition, Phase 2 elements P2E4 and P2E6 would provide Kow and/or K values for use in this element.

oc

P3E4 Environmental Concentrations - Sediment

Rationale

This element describes the concentrations of chemicals in sediment in Ontario. Unlike Phase 3 elements for concentrations in other environmental compartments, the link between concentrations of chemicals in sediment and human exposure is rather indirect. However, a tentative relationship between sediment and fish can be developed assuming the fish are subsequently available for consumption.

Scoring Criteria

As in the other Phase 3 environmental concentration elements, the scoring criteria for sediment concentrations are normalized relative to human exposure. A 60 kg individual is assumed to consume 0.022 kg per day of sport fish caught in Ontario (Cox *et al.*, 1985). To achieve a daily exposure of 100 ug/kg/day would require that the fish contain at least 270,000 ug of chemical/kg fish (100 ug/kg/d X 60 kg/0.022 kg/d).

The criteria for sediment are based on the adsorption coefficient (Kp) and bioconcentration factor (BCF). The Kp for a substance can be expressed as the concentration in sediment divided by the concentration in water. The BCF is the concentration in fish divided by the concentration in water. These two expressions can be rearranged and the Kp expression substituted into the BCF equation to produce the expression

$$\text{Concentration in fish} = \text{BCF} \times \text{concentration in sediment} / K_p$$

As noted in element P2E6, BCF can be estimated from Kow values. Similarly, Kp values can be estimated from Kow data (see Lyman *et al.*, 1982). Based on the assumption that sediment contains 4% organic carbon and that fish contain 270,000 ug/kg (calculated above as the level required to attain a score of ten), the sediment concentrations that would result in a score of ten range from approximately 20,000 ug/kg for a substance with a log Kow of 2 to 110,000 ug/kg when log Kow is 5. The simplistic approach used to calculate these values and the indirect nature of the link between sediment concentrations and human exposure make it somewhat superfluous to assign scores for various ranges of Kow. Accordingly, concentrations of 50,000 ug/kg or more (on a wet weight basis) are assigned a score of 10 for all substances. As with similar elements, scores decrease by two for each ten-fold decrease in observed concentrations.

The information regarding the concentrations of chemicals in sediment would be derived from (in order of preference), a) concentrations measured in Ontario; b) concentrations estimated

using environmental modeling techniques; or c) data from outside Ontario. Even for data gathered in Ontario, most measurements of sediment concentrations have been collected from areas near major sources, so that they may not be representative of larger areas. Modeling techniques could be used to estimate average concentrations over wide areas.

Information from these sources are then used in the assignment of scores for this element as follows:

ELEMENT SCORE	SEDIMENT CONCENTRATION or DETECTION LIMIT (ug/kg)
10	⁴ 5x10 ³ ⁴
8	>5x10 ³ - 5x10 ⁴
6	>500-5x10 ³
4	>50-500
2	≥5-50
0	<5

Suggested Information Sources

Phase 2 element P2E6 should provide Kow values. Other sources of data on the concentrations of chemicals in sediments included MOE sediment monitoring studies, sediment monitoring studies reported by the IJC Great Lakes Water Quality Board, Surveillance Working Group and the Upper Lakes Reference Group, and Sediment surveys undertaken by Environment Canada.

P3E5 Environmental Concentrations - Plants

Rationale

This element describes the concentrations of chemicals in plants grown in Ontario or imported into Ontario for consumption. Aquatic and terrestrial plants are considered, particularly those used as foods. The assessment of the potential exposure to chemicals as a result of consumption of plant material is based on information on the concentrations of chemicals in plants.

Scoring Criteria

As outlined in the general rationale, the scoring criteria for concentrations of chemicals in plant material are normalized relative to human exposure. A 60 kg individual is assumed to consume one kg of plant material per day. Food consumption data

(Nutrition Canada, 1977) indicate that the average Canadian male aged 20 to 39 years consumes 0.6 kg of vegetables and fruits per day and about 0.3 kg of cereals. Similar data are available from international assessments (WHO, 1985). Based on these data, it is assumed that one kg of plant material per day should represent or exceed the typical daily intake by Ontario residents. Therefore, plant concentrations of 6000 ug/kg fresh weight $[(100 \text{ ug/kg} \times 60 \text{ kg}) / (1 \text{ kg/d})]$ or more are assigned scores of ten.

The information regarding the concentrations of chemicals in plant material are derived from (in order of preference), a) concentrations measured in plant material grown in Ontario; b) concentrations estimated in plant material using environmental modeling techniques; or c) data from outside Ontario. For data gathered in Ontario, many measurements will have been taken of plants known or suspected to have received relatively large exposures so that they may not be representative of larger areas. Modeling techniques could be used to estimate average concentrations over wide areas.

Information from these sources are used in the assignment of scores for this element as follows:

ELEMENT SCORE	CONCENTRATION IN PLANTS or DETECTION LIMIT (ug/kg)
10	$>6 \times 10^3$
8	$>6 \times 10^2 - 6 \times 10^3$
6	$>60 - 6 \times 10^2$
4	$>6 - 60$
2	$\geq 0.6 - 6$
0	<0.6

Suggested Information Sources

Data regarding the concentrations of chemicals in plant materials are available from MOE and Environment Canada monitoring data, Health Protection Branch market basket survey data, Agriculture Canada monitoring data, EPA monitoring data, and U.S. Food and Drug Administration food monitoring data.

P3E6 Environmental Concentrations - Animals

Rationale

This element describes the concentrations of chemicals in animal products produced or imported for consumption in Ontario (including meats, poultry, eggs, cheese, milk, fish and other aquatic animals). Both aquatic and terrestrial animals are considered, particularly those used as foods. Information regarding the concentrations of chemicals in animals is critical to the assessment of potential exposures since animal products consumed as food result in direct exposure.

Scoring Criteria

As outlined in the general rationale, the scoring criteria for concentrations of chemicals in animals and animal products are normalized relative to human exposure. The scoring criteria assumes an average 60 kg individual consuming about one kg of animal products per day. Food consumption data (Nutrition Canada, 1977) indicate that the average Canadian male aged 20 to 39 years consumes about 0.3 kg of meat, poultry, and eggs per day plus an additional 0.4 kg of dairy products per day. Commercial fish consumption averages about 0.022 kg per day. Certain populations may have considerably higher rates of fish consumption and lower rates of consumption of other animal products. Based on these data, it is assumed that one kg of animal products per day should represent or exceed the typical daily intake by Ontario residents.

Assuming a consumption rate of 1 kg/day, chemical concentrations of 6000 ug/kg of animal produce ($100 \text{ ug/kg} \times 60 \text{ kg}$)/(1 kg) or more are assigned scores of 10. As with other environmental concentration elements, scores decrease by two for each ten-fold decrease in concentration.

Information on the concentrations of chemicals in animals would be derived from (in order of preference), a) concentrations measured in animals in Ontario; b) concentrations estimated using environmental modeling techniques; or c) data from outside Ontario. Even for data gathered in Ontario, many measurements may have been made of animals thought to have received above average exposures so that the data may not be representative of larger areas. Modeling techniques could be used to estimate average concentrations for wide areas.

Information from these sources are used to assign scores for this element as follows:

ELEMENT SCORE	CONCENTRATION IN ANIMALS or DETECTION LIMIT (ug/kg)
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10	$>6 \times 10^3$
8	$>6 \times 10^2 - 6 \times 10^3$
6	$>60 - 6 \times 10^2$
4	$>6 - 60$
2	$\geq 0.6 - 6$
0	< 0.6

Suggested Information Sources

Information on the concentrations of chemicals in animals and animal products would be available from monitoring data gathered by the MOE, Ontario Ministry of Agriculture and Food or Ministry of National Resources, Environment Canada monitoring data, Health Protection Branch market basket survey data, Agriculture Canada monitoring data, EPA monitoring data, and U.S. Food and Drug Administration monitoring data.

6.2 Element Describing The Frequency of Environmental Dispersion

Phase 3 element P3E7 was selected to provide input into the scoring system for the frequency with which the dispersion of chemicals occurs. This factor is important in assessing the impact of chemicals on the environment and health and, therefore, in the assignment of priorities to the regulatory assessment of groups of chemicals. Element P3E7 provides an estimate of the actual frequency of environmental dispersion, not the frequency or amount of analytical data available on concentrations of the chemical in the environment.

P3E7 FREQUENCY OF DISPERSION

Rationale

This element describes the frequency of dispersion of chemicals into the environment in terms of release frequency. Important factors in evaluating the potential hazard to the environment and health from a chemical are the frequency and duration of exposure. Elements P3E1 through P3E6 provide input into the scoring system of the levels of chemicals in the environment. At

a given toxic potency and level in the environment, the hazard posed by a chemical increases directly with the frequency and duration of exposure.

Both the frequency and duration of exposure are dependent on the frequency of dispersion or release of the chemical into the environment. The more frequent the release of the chemical, the greater the frequency of exposure and the longer its duration. Therefore, release frequency is used in the vector system as a surrogate for exposure frequency and duration.

Scoring Criteria

The scoring criteria for this element are based on the number of days during the year when the chemical is released. Any release, no matter how short, occurring in one 24 hour period is considered a release-day. For the purpose of scoring it is generally assumed that the grouping of release-days is not critical (i.e. they could be sequential, or sporadic in spacing throughout the year). If in the view of the user, however, the grouping of the release-days is critical to the assessment of the chemical, appropriate adjustments to the scoring should be made.

Both intentional and unintentional releases are considered equally. A chemical released into the environment through use, where usage is more or less continuous would score 10 (e.g. chemicals in automobile exhaust emissions). Chemicals with seasonal use with between 150 and 300 release days/year would score 8 (e.g. pesticides used seasonally). Chemicals normally contained in closed systems where venting of containers may occur periodically would score 2 to 4, depending on the frequency of venting.

The scoring criteria used are outlined in the following table:

ELEMENT SCORE	CRITERIA (release-days/year)
10	>300
8	>150 to 300
6	>50 to 150
4	>10 to 50
2	≥1 to 10
0	<1

Suggested Information Sources

The information for the determination of the release frequencies will have to be derived from knowledge of how the chemical is used and dispersed in the environment. Some of this information is provided by other elements in the Phase 3 vector (e.g. concentrations in air, water, soil/sediment, animals and plants).

6.3. Elements Describing Properties Affecting Toxicity

Elements P3E8 through P3E14 were selected to describe the toxicological properties of chemicals in Phase 3 of the scoring system. Information on acute lethality of chemicals to all targets in the environment is included in element P3E8. The sub-lethal effects of chemicals on ecological systems (plants and animals) are described in elements P3E9 and P3E10. Elements P3E11 through P3E14 are primarily designed to describe potential adverse effects on human health.

When data are lacking on the effects of a chemical on a specific environmental target (e.g. humans, fish or wildlife) the best available information should be used. Unless specific data are available on species differences in responses to the chemical, it is assumed that all species respond in an equivalent manner and the most sensitive would be used in scoring. Differences in response among species, or other differences between experimental and "real-world" exposure situations (e.g. data from high level experimental exposures extrapolated to much lower levels) are not considered in Phase 3. Such considerations were viewed as beyond the sophistication of a general scoring system and would be evaluated as part of the subsequent detailed regulatory assessment for chemicals scoring high in Phase 3.

There are several general topics, including route and duration of exposure and validity of testing procedures, that apply equally to all of the toxicity elements. These are discussed below and will only be briefly referred to in the descriptions of each element.

6.3.1 Route of Exposure

Route of exposure was identified in Phase 2 as an important factor in the judgment of the applicability and validity of the effects observed under controlled experimental conditions (Grice, 1984; Willes *et al.*, 1985). These considerations are of greater importance in Phase 3 where more complex effects of chemicals are considered. In terrestrial animals, oral, inhalation and dermal routes of exposure are considered the most representative of "real-world" exposures. In aquatic species, the usual route of exposure is through water. In plants, exposures usually occur through soils or from the atmosphere. In all test systems, data derived by direct application of chemicals to biological systems (e.g. direct injections into tissues) that by-pass normal

absorption and uptake systems may indicate the potential for the production of adverse effects but their relevance to normal exposures should be carefully evaluated. In addition, the use of vehicles (e.g. dimethylsulfoxide) in dermal exposure studies can substantially increase the uptake of chemicals through the skin and, although the results would indicate a worst-case assessment of potential effects, their relevance to usual dermal exposure is questionable. In all of the toxicity elements the scorer must exercise judgment in the use of data derived from unusual exposure routes. If such data are the only information available it may be used, but the scores assigned require appropriate modifiers(e .g., ? or ! or "e").

6.3.2 Duration of Exposure

The duration of exposure is important in the assessment of potential effects of chemicals on the environment and health (Hushon and Kornreich, 1984). As outlined in Phase 2, acute lethality is usually assessed following a single exposure (e.g. LD50, LC50), or following a short duration of exposure (e.g. acute tolerance tests or 96-hour LC50 tests in aquatic species). The assessment of long term effects usually involve multiple exposures for the major portion of the life-span of the test system (FDA, 1982). This is usually considered a minimum of one year in terrestrial animals (FDA, 1982), but may be as short as a few days in certain short-lived aquatic and plant test systems.

In the assessment of long term effects of chemicals, judgment is required to determine if the duration of exposure and observation in the studies was adequate both to achieve a steady state level of the chemical in the system and to encompass the latency period for the development of adverse effects. The biological half-life of the test chemical can assist in judging whether steady state levels of the chemical in the test system were achieved. For example, a minimum of 3.5 half-lives are generally required to reach 99% of the steady state body burden (FDA, 1982; Willes et al., 1985).

The latency period between the initiation of exposure and the development of particular adverse effects depends on the type of effects produced, in addition to the time required to achieve a steady state body level. Effects related to general narcotic actions of chemicals generally have much shorter latency periods (e.g. several hours) compared to cancer where latency periods range from months to years (Grice et al., 1984; Willes et al., 1985).

If adequate long term exposure data are not available, scores for toxicity elements addressing long term effects may be estimated from shorter term exposure data. In terrestrial animals, data from exposures of 90 days may provide reasonable estimates of certain long-term effects, although the validity of extrapolating such data to predict chronic effects requires considerable

judgment. Judgment is even more critical when estimates of potential chronic effects are made by extrapolation of data from various short-term in vivo or in vitro test systems (Grice, 1984; Willes et al., 1985). It is not possible nor desirable to overly complicate a scoring system by incorporating all the uncertainties of extrapolating data from shorter to longer exposure scenarios. Such details are left to the subsequent regulatory assessment of high priority chemicals selected from Phase 3. Therefore, as a general rule, when effects related to long term exposure are estimated from short term exposure data, the scores derived require appropriate modifiers (e.g. (!), (?) or "e") indicating uncertainty in the assigned score.

6.3.3 Validity of Testing Procedures

The assignment of scores to the various toxicity elements requires that the scorer assess the validity of the procedures followed in the collection of the toxicological data. It is beyond the scope of this scoring system to provide details of adequate procedures for the myriad of ever-changing tests available. The following references outline current standard procedures used in the collection of toxicological data: Grice et al. (1975); IARC (1980a); FDA (1982); EPA (1984); NTP (1984); OSTP (1985). The validity of new testing procedures can usually be determined from publications by recognized authority centres around the world (e.g. Health and Welfare Canada, U.S. EPA, U.S. FDA, WHO, OECD, IARC).

P3E8 ACUTE LETHALITY

Rationale

Element P3E9 describes the acute lethality of a chemical to terrestrial and aquatic animals. The general rationale for the acute lethality element is as outlined in Phase 2 element P2E7 but the criteria are expanded. Non-lethal or reversible effects are not included in this element. An element addressing the acute lethal effects of chemicals is needed in the Phase 3 vector to ensure that chemicals with high levels of acute toxicity are adequately considered in the regulatory process.

Acute effects other than lethality (e.g. irritation, allergic reactions, general narcosis, etc.) are considered in other toxicity elements in Phase 3. As in Phase 2, criteria for phytotoxicity are not included in this element because of the difficulties in assessing lethality in plants. Effects in plants, both lethal and non-lethal, are included in the criteria for element P3E10.

Scoring Criteria

Scoring criteria for acute oral and dermal LD50s and inhalation and aquatic LCs are similar to those utilized by the Trans-

portation of Dangerous Goods Act (Transport Canada, 1984) and the State of Michigan Critical Materials Registry (1979). Scores of six down to zero for oral and dermal LD50s are comparable to the extremely toxic to relatively non-toxic scales outlined in the literature (Hodge and Sterner, 1949; Gleason *et al.*, 1977, Doull *et al.*, 1980). The criteria for scores of 8 to 10 would identify chemicals with greater toxicity than in those included in the scales referred to above. These more stringent criteria were adopted to ensure chemicals with extreme acute lethality are clearly identified by the scoring system.

The scoring criteria for inhalation LC50s are derived from the oral LD50 criteria, assuming a 60 kg individual respires 20 m³ of air daily and that the contaminants have equal biological availability via the oral and inhalation routes of exposure. The aquatic toxicity LC50 data would usually be derived from 96-hour exposures.

Scoring criteria for this element are as follows:

ELEMENT SCORE	CRITERIA			
	Oral LD50 mg/kg	Dermal LD50 mg/kg	Inhalation LC50 mg/m ³	Aquatic LC50 mg/L
10	≤0.5	≤0.5	≤1.5	≤0.1
8	>0.5-5	>0.5-5	>1.5-15	>0.1-1
6	>5-50	>5-50	>15-150	>1-10
4	>50-500	>50-500	>150-1500	>10-100
2	>500-5000	>500-5000	>1500-15000	>100-1000
0	>5000	>5000	>15000	>1000

Suggested Information Sources

AQUIRE database

- This database contains acute lethality values for aquatic and terrestrial species.

Hayes, 1982

- Contains information on the toxicology of pesticides and associated chemicals with particular reference to effects in humans.

Ketchen *et al.*, 1979

- These Critical Material Data sheets summarize information on the toxic potential of individual chemicals, including acute lethality data, in terrestrial species.

Merck Index

- The Merck Index lists indices of toxicity for many chemicals in terrestrial species.

MEDLINE database

- A computerized database presenting titles and abstracts of published, worldwide, biomedical literature.

Clayton & Clayton, 1981

- Summarizes the toxic characteristics of a large number of industrial chemicals, primarily in terrestrial species.

P3E9 SUB-LETHAL EFFECTS ON NON-MAMMALIAN SPECIES

Rationale

This element describes potential effects from long-term exposures of non-mammalian species to chemicals. The effects-data may be expressed as median effect concentration (EC50), maximum aquatic toxic concentration (MATC) or no-observed-adverse-effect-concentration (NOAEC).

The most frequently reported data of these types are EC50 values for fish or other aquatic organisms such as daphnia. Associated with an EC50 value is the species studied, the endpoint(s) observed, and the duration of exposure. Common endpoints are immobilization, loss of equilibrium, effects on reproduction and other sub-lethal effects. As with other elements, if different indicators of effects are available, the most sensitive would be used, unless scorer judgment indicates otherwise.

As with mammalian toxicity, duration of exposure is important to the interpretation of the results. For aquatic organisms, either full or partial life-cycle tests are preferred for the assessment of reproductive effects. Such tests may last as few as seven days or extend beyond a year depending on the life cycle. For terrestrial animals, periods of exposure usually last several months. For other types of effects, results from 96-hour exposures generally have more credence than shorter exposures. In addition, preference should be given to tests on freshwater species native or introduced to North America.

Scoring Criteria

Based on published results of the effects of many substances on aquatic organisms, the NOAEC values that appear in the score definitions are a factor of 100 lower than EC50 values. Maximum Aquatic Toxic Concentration (MATC) values are 10 times lower than EC values (Konemann and Viser, 1983).

The scoring criteria for this element are as follows:

ELEMENT SCORE	CRITERIA	
	Aquatic Organisms	Terrestrial Organisms
10	EC50 \leq 0.02 mg/L; OR MATC \leq 0.002 mg/L; OR NOAEC \leq 0.0002 mg/L in different genera.	Adverse effects at \leq 1 mg/kg for subchronic exposure OR \leq 0.5 mg/kg for chronic exposure, in different genera.
8	EC50 \leq 0.02 mg/L; OR MATC \leq 0.002 mg/L; OR NOAEC \leq 0.0002 mg/L in one genus only.	Adverse effects at \leq 1 mg/kg for subchronic exposure OR \leq 0.5 mg/kg chronic exposure, in one genus only.
6	EC50 $>$ 0.2-0.02 mg/L; OR MATC $>$ 0.02-0.002 mg/ OR NOAEC $>$ 0.002-0.0002 mg/L	Adverse effects at $>$ 1 - 10 mg/kg for sub- chronic exposure OR $>$ 0.5 - 5 mg/kg mg/kg for chronic ex- posure.
4	EC50 $>$ 2-0.2 mg/L; OR MATC $>$ 0.2-0.02 mg/L; OR NOAEC $>$ 0.02-0.002 mg/L.	Adverse or non-adverse effects at $>$ 10 - 100 mg/kg for sub-chronic exposure OR $>$ 5 - 50 mg/kg for chronic exposure
2	EC50 $>$ 20-2 mg/L; OR MATC $>$ 2-0.2 mg/L; OR NOAEC $>$ 0.2-0.02 mg/L.	Adverse or non-adverse effects at $>$ 100 - 1000 mg/kg for sub-chronic exposure OR $>$ 50 - 500 mg/kg for chronic ex-
0	EC50 $>$ 20 mg/L; OR MATC \geq 2 mg/L; OR NOAEC \geq 0.2 mg/L.	\geq 1000 mg/kg for sub- chronic exposure, \geq 500 mg/kg for chronic exposure.

Suggested Information Sources

AQUIRE database

- AQUIRE has EC50 and/or NOAEC data for aquatic organisms for some organic chemicals.

Brooke et al., 1984-85

-Acute toxicities of organic chemicals to fathead minnows (Pimephales promelas). Center for Lake Superior Environmental Studies, University of Wisconsin-Superior, Superior, Wisconsin (2 volumes).

Most information required for this element must be sought from primary sources identified through literature searches.

P3E10 SUB-LETHAL EFFECTS ON PLANTS

Rationale

Element P3E10 describes the effects of chemicals on plants. Sub-lethal effects on plants are highly varied depending on the toxicant. The relative significance of the injury or effects depends on the commodity and its use. These can be divided into three categories.

- a) Situations where effects are on the appearance of the plant. Such effects are relevant for ornamentals, flower crops, leafy vegetables and fruits. Effects on growth and yield are much less important under these circumstances.
- b) Situations where the impact on growth and yield are the most significant, and visible injury to the foliage though unsightly, is of less importance. Such effects are significant for vegetables, fruits, seeds and storage organs (e.g. tubers).
- c) Situations where there are no visible injurious effects, but the longevity of the commodity has been altered. Such effects are of greatest significance in flower crops and storage fruits and vegetables.

The toxic effects can generally be assessed using short term tests with indicator plants. The possible effects encompass a wide spectrum of responses; including inhibition of germination, inhibition of seedling growth; growth abnormalities; reduction in either root or shoot growth. Long term tests with annual plants may be used to assess chronic effects, such as decreased yield or decreased competitiveness (NAS, 1975).

The most commonly tested aquatic plants are algae and duckweed (Lemna minor) (U.S. EPA, 1978). Several test methods have been developed that use algae (e.g. the EPA Algal Assay Bottle Test).

Duckweed has been used to assess the effects of substances on aquatic macrophytes (U.S. EPA, 1978).

Effects on the genetic make-up of the organism may be assayed using other short term tests with plant material. These include gene mutations, DNA repair, primary DNA damage and chromosomal aberrations (Sandhu, 1980). Some examples of genetic-effects assays using plants are the measurement of chromosomal aberrations in root tip cells, the Tradescantia micronucleus assay (Sandhu, 1980) and the use of Arabidopsis for measuring the frequency of mutational events at the embryo stage (Redei, 1980).

Scoring Criteria

The score definitions for aquatic plants are very similar to those used in P3E9 for sub-lethal effects on aquatic animals.

Chemical effects on plants may be placed in three different categories, and the scoring criteria will vary according to the effect.

- a) Those substances that are toxic to plants but with no carry-over effects on animals (e.g. O_3 , NO_x , SO_2).
- b) Those substances that are toxic to plants, accumulate and are toxic to animals (e.g. F, Cd, Zn).
- c) Those substances that are non-toxic to plants, but accumulate and are toxic to animals (e.g. Pb, Cr).

Categories b) and c) above are covered in other elements in the scoring system and the focus of this element will be on category a) only.

Various biomonitors have been used for different contaminants with each species displaying characteristic symptoms for a given pollutant. Some of these tests have been standardized to a substantial degree, while others are only qualitative indicators. Standardized sampling methods have also been devised for substances that accumulate in vegetation and that are toxic to animals. Lichens are also used for a variety of contaminants, both as indicator by presence or absence, or are used as accumulators.

Standardized tests have been reported for relatively few substances. The scoring criteria accommodate results expressed in concentration units (e.g. mg/L for substances in water, $\mu g/m^3$ for gaseous contaminants, and mg/kg for substances in soils), however, in most instances the length of exposure time is also very important. Duration of exposure is not considered in this element, however, other elements in the scoring system address the characteristics of the chemical that affect duration of exposure (e.g. environmental persistence, the number of releases,

concentrations in various environmental compartments.

As emphasized in the Michigan Critical Materials Register (1986), the validity of developing numerical criteria for scoring the phytotoxic effects of chemical can be questioned due to the wide variation in responses of plants to toxicants, the lack of standardized testing procedures and the difficulties in extrapolating from one exposure situation to another. In addition, results will likely be available for relatively few substances. However, numerical criteria are presented for this element as a general guide to future data that will hopefully become available in this area. In addition, general descriptive criteria are included for use if numerical data are not available. As with other elements in Phase 3, score modifiers (e.g. !, ?, e) should be used to indicate the confidence in the score assigned.

Studies on terrestrial plants conducted in greenhouses must be interpreted with caution since greenhouse environments may be considerably different from field conditions. Caution is also necessary when interpreting soil extraction procedures to determine the level of a toxicant. For example, the total amount removed by acid extraction may not be meaningful in relation to plant bioavailability.

The scoring criteria for this element are as follows:

ELEMENT SCORE	AQUATIC PLANTS		TERRESTRIAL PLANTS		GENERAL NARRATIVE
	EC50	NOAEC	EC50	NOAEC	
10	<0.01w	<0.001w	<0.01w <10a <0.1s	<0.001w <1a <0.01s	Irreversible dysfunctional pathological effects
8	0.01-0.1w	0.001-0.01w	0.01-0.1w 10-100a 0.1-1s	0.001-0.01w 1-10a 0.01-0.1s	Reversible dysfunctional pathological effects
6	>0.1-1w	>0.01-0.1w	>0.1-1w >100-1000a >1-10s	>0.01-0.1w >10-100a >0.1-1s	Degenerative, reversible effects slightly dys- functional
4	>1-10w	>0.1-1w	>1-10w >1000-10000a >10-100s	0.1-1w >100-1000a >1-10s	Reversible eff- ects, not dys- functional

ELEMENT SCORE	AQUATIC PLANTS		TERRESTRIAL PLANTS		GENERAL NARRATIVE
	EC50	NOAEC	EC50	NOAEC	
2	>10-100w	>1-10w	>10-100w >1X10 ⁴ -1X10 ⁵ a >100-1000s	>1-10w >1000-1X10 ⁴ a >10-100s	Reversible effects such as enzyme induction and sub-cellular effects
0	≥100w	≥10w	≥100W ≥1X10 ⁵ a ≥1000s	≥10w ≥1X10 ⁴ a ≥100s	No effects measurable

w = concentration of substance in water in mg/L
a = concentration of substance in air in mg/m³
s = concentration of substance in soil in mg/kg

Suggested Information Sources

Phytotox database

- Contains NOAEC data for some substances in terrestrial plants.

AQUIRE database

- Contains EC50 and/or NOAEC data for some substances in aquatic plants.

Manning, W.J. and Feder, W.A. 1980

- Biomonitoring Air Pollutants with Plants, London: Applied Science Publishers. 142p.

Lepp, N.W., (ed.). 1981.

- Effects of heavy metal pollution on plants. Vol. 1 and 2. London: Applied Science Publishers. Vol 1, 257 p.; Vol 2, 353 p.

Martin, H.M. and Coughtrey, P.G. 1982.

- Biological monitoring of heavy metal pollution. Land and Air. London: Applied Science Publishers. 475 p.

Levitt, J. 1980.

- Responses to plants to environmental stresses. Vol. II. Water, Radiation, Salt and other Stresses. Academic Press. 606p.

Ormrod, D.P. 1978

- Pollution in Horticulture. Elsevier Scientific Publishing Co. 260 p.

NRCC Publications

- The National Research Council Canada, Environmental Secretariat, published a number of reviews of the effects of various substances on the environment. Most of these publications contain information on the effects of the substance reviewed on plants.

Most information required for this element must be sought from primary sources identified through literature searches.

P3E11 SUB-LETHAL EFFECTS ON MAMMALS

Rationale

This element describes potential longer-term effects of chemicals in mammals. The effects are directed primarily at human health, although the actual data used will largely be from laboratory animals. Other scoring systems (see Hushon and Kornreich, 1984) generally score chemicals for sub-lethal toxicity based on specific effects (e.g. separate scores for carcinogenicity, mutagenicity, teratogenicity, etc.), but most do not address systemic toxic effects. The toxic effects included in this element are restricted to sub-lethal systemic effects, but do not include carcinogenic, mutagenic or teratogenic effects since these are included in other Phase 3 elements.

Scoring Criteria

If data are not available on the effects following a suitable duration of exposure, either appropriate "tags" (!, ? or e) should be used, or, preferably, the criteria would be divided by an appropriate extrapolation factor to adjust for potential effects that would not develop during shorter exposure studies. Criteria used in the development of scores for this element would be derived from sub-chronic (generally 90-day exposure) or chronic (usually 1 year or more) exposure studies in any mammalian species (Refer to the general discussion of exposure duration, Section 6.3.2). If the data were derived from sub-chronic studies, it is recommended that the NOAEL be divided by a 10-fold extrapolation factor (see FDA, 1982, Dourson and Stara, 1983). If the only data available involved even shorter term exposures (e.g. 14 days), it is recommended that a 100-fold extrapolation factor be used. Considerable judgment will be required in the utilization of such extrapolation factors, considering issues such as the biological half-life of the chemical, the biological characteristics of the test system from which the data was derived and knowledge of the usual consequences of the type(s) of lesions produced.

The scoring criteria for this element do not provide for differences in the type of toxic response observed. For example, if the effects associated with exposure are irreversible, the

consequences of exposure are much more serious than if the effects reverse following cessation of exposure. For the purposes of Phase 3, all effects are considered as equal and details of differences in the severity of the effects would be carefully considered in the regulatory evaluation of specific chemicals following Phase 3 prioritization.

Examples of the various end-points included as chronic systemic effects are as follows (previously outlined in for Phase 2 element P2E8):

- | | |
|-----------------------|--|
| Reproduction toxicity | - Adverse effects on reproduction as they affect the survival, development and well-being of the species, including interference with gonadal functions but excluding teratogenic effects. |
| General Toxicity | <p>- General depressions in body weight and body weight gains, general behavioral alterations and increases in diseases secondary to chemical exposure.</p> <p>- Gross or microscopic alterations indicative of disease from toxic events.</p> <p>- Adverse or deleterious effects on organ systems or functions, alterations in secretions of exocrine and endocrine glands, alterations in the brain and peripheral nervous systems.</p> <p>- Treatment related biochemical effects.</p> |

If data are available on more than one of these effects, the effect occurring at the lowest exposure level in the most sensitive test system would be used in scoring. In addition, structure-activity relationships may provide estimates of the occurrence of chronic effects if data on the actual compound are lacking (see Appendix C). Structure-activity relationships appear reasonably predictive for certain types of effects (e.g. narcotic effects), however, little predictive value is obtained for other effects using available methods. In the future, the accuracy of structure-activity relationships in predicting effects between different chemicals may improve. Even with present methodologies, however, an estimation of potential effects may prove more valuable than accepting a judgment of inadequate information. Such estimates, however, would be appropriately modified with a ? or "e".

The scoring system for this element is as follows:

ELEMENT SCORE	CRITERIA ^a	
	Oral NOAEL mg/kg body weight	Inhalation NOAEL mg/m ³ b
10	≤0.1	≤0.3
8	>0.1-1	>0.3-3
6	>1-10	>3-30
4	>10-100	>30-300
2	>100-1000	>300-3000
0	>1000	>3000

a
Criteria are based on data from exposures of 1 year or more in duration. If data from studies of 28 to 90-days exposure are used, divide all scoring criteria by 10. If data from 14-day studies are used, divide all scoring criteria by 100.

b
 $\text{mg/m}^3 = [\text{ppm} \times \text{molecular weight} \times 0.92]/22.4$

Suggested Information Sources

Most of the information on the toxic effects associated with chronic exposure to chemicals would be obtained from original scientific publications which could be accessed through the MEDLINE and TOXLINE databases. Additional sources of summary data include Ketchen *et al.* (1979), Clayton and Clayton (1981), RTECS database, and Verschueren (1983). It should be emphasized, however, that the judgment of the validity of a NOEL from summary data is difficult and that original publications should be consulted.

P3E12 TERATOGENICITY

Rationale

This element describes the potential teratogenic effects of chemicals on mammalian systems. Toxic effects on reproduction in plants, non-mammalian and mammalian systems, as distinct from developmental defects, are described in Phase 3 elements P3E9, P3E10 and P3E11. The production of terata by exposure to chemical contaminants can seriously compromise the development and survival of offspring. Such effects are usually irreversible, although current understanding is that they have an exposure threshold (EPA, 1984).

The criteria for these effects are as outlined by the US Environmental Protection Agency (EPA, 1984). Teratogenic effects include frank developmental malformations detrimental to the survival, future development, or well-being of newborn. They do not include developmental anomalies and aberrations that appear to be secondary to embryo-, feto- and maternal toxicity (see EPA, 1984; Khera, 1981). Many such effects are known to recover as development proceeds (e.g. reversible delayed ossification of various parts of the skeleton, delayed development of specific organs, delayed eye opening, delayed vaginal opening, reduced body weight) (Khera, 1981). In some cases, exposure of pregnant females to chemicals can result in malnutrition due to decreased feed intake. Malnutrition has been shown to delay embryo and fetal development, reduce birth weights and, in severe cases, produce irreversible neurological and metabolic abnormalities (EPA, 1984; Khera, 1984). These differences in the apparent severity between frank terata and minor developmental anomalies from chemicals are reflected in the scoring criteria for this element.

Behavioral teratology is a rapidly developing sub-field of teratology and includes effects related to alterations in the behavior of the offspring as they mature. In some cases behavioral effects may not be evident until maturity (e.g. effects on sexual behavior). Other effects may only be temporary and actually disappear at some later stage of development. No specific criteria have been included in this element for behavioral teratogenic effects and judgment must be exercised to determine how such effects "fit" into the criteria provided. As the significance of such effects is better understood, alterations in the criteria for this element may be required to encompass the increase in knowledge.

Scoring Criteria

Working from the assumption that teratogenic effects exhibit exposure thresholds (Khera, 1981; EPA, 1984), scoring criteria are based on gradations in exposure levels associated with effects. Since teratogenic effects are viewed as more serious than developmental anomalies as outlined above, higher scores are applied to chemicals showing evidence of frank teratogenicity. Chemicals producing developmental anomalies and aberrations are assigned lower scores (e.g. delayed ossification of bone, decreased fetal weights, decreased birth weights, prolonged gestation, decreased survival without abnormalities, developmental effects that reverse during postnatal development).

Duration of exposure is particularly critical in assessing teratogenic effects. To adequately assess the potential for such effects from a chemical exposure should occur at least through the period of organogenesis (e.g. usually from late in the first trimester through early in the third trimester of gestation). In addition, the levels of exposure studied should be sufficient to

elicit a range of effects in the dams, from toxicity at the higher exposures to no-observable effects at the lower exposures (Grice et al., 1975; EPA, 1984; Khera, 1984).

The general requirements regarding route of exposure discussed in Section 6.3.2 also apply to teratogenicity assessments.

The scoring criteria for this element are as follows:

ELEMENT SCORE	CRITERIA
10	- Teratogenic effects observed without overt maternal toxicity at maternal exposures ≤ 0.1 mg/kg/day during organogenesis, or equivalent ^a .
8	- Teratogenic effects observed without maternal toxicity at maternal exposures $>0.1-1$ mg/kg/day during organogenesis or equivalent exposure.
6	- Teratogenic effects or developmental anomalies observed at maternal exposures $>1-10$ mg/kg/day during organogenesis or equivalent.
4	- Teratogenic effects or developmental anomalies observed at maternal exposures $>10-50$ mg/kg/day during organogenesis or equivalent exposure.
2	- Teratogenic effects or developmental anomalies observed at maternal exposures $>50-1000$ mg/kg/day during organogenesis or equivalent exposure.
0	- No terata observed at observed at maternal exposures ≥ 1000 mg/kg/day or equivalent.

^a Equivalent exposure by inhalation or dermal routes, assuming effects by dermal exposure would occur at comparable doses to oral exposure and that the total dose by inhalation is equivalent to oral exposure based on a 60 kg adult respiring 20 m³ of air daily. These assumptions mean that the dermal and oral exposure levels are equivalent, and inhalation exposures (in mg/m³) are obtained by multiplying the oral exposure by three.

Information Sources

Most of the information on the teratogenic effects associated with exposure to chemicals would be obtained from original scientific publications which could be accessed through the MEDLINE and TOXLINE databases. Additional sources of summary data include Ketchen et al., (1979), Clayton and Clayton, 1981,

RTECS database, and Verschueren, 1983. Care should be exercised in using the RTECS data base since only studies showing positive effects associated with exposure are reported. It must also be emphasized that the judgment of the validity of teratogenic effects (e.g. the evaluation of frank developmental anomalies versus developmental aberrations) from summary data is difficult and that original publications should be consulted.

P3E13 GENOTOXICITY/MUTAGENICITY

Rationale

This element describes the mutagenic and genotoxic potential of a chemical. Such effects in themselves are indicative of potential hazards of chemicals to health and the environment. In addition, the strength of such evidence is valuable in the interpretation of other potential hazards from chemicals (e.g. carcinogenicity).

Genotoxic or mutagenic effects on somatic or germ cells are considered equal potential hazards. Evidence of heritable mutations (i.e. mutations in germ cells) was regarded as more indicative of the test system studied and ability of a chemical to distribute to germ cells (i.e. the disposition of the chemical in vivo) rather than of a greater potential hazard. In addition, assessment of the potential for germ cell mutations requires specific tests (e.g. dominant lethal test, mouse heritable translocation assay) and results from such tests would not likely be available for large numbers of chemicals. Therefore, specific scoring criteria for germ cell mutations would increase the dependency of the resulting prioritization of chemicals on the information available rather than indicators of potential hazard. In the scoring criteria used, chemicals for which evidence of germ cell mutations are available would receive high scores, however, not preferentially higher than chemicals with evidence of somatic mutations only.

Scoring Criteria

The criteria assign higher scores to chemicals with adequate evidence of mutagenic/genotoxic effects derived from short-term tests. The primary objective is to score the potential of a chemical to produce such effects. Assessment of the actual risk of occurrence of these effects is beyond the sophistication of the current scoring system and would be addressed during detailed regulatory assessment of high priority chemicals identified in Phase 3.

Chemicals producing direct mutagenic/genotoxic effects in the absence of overt toxicity are assigned the highest scores (e.g. the chemical or its activate metabolite(s) directly acts on genetic material to produce mutations or genotoxic effects). Clastogenic effects produced by chemicals that do not directly interact with genetic material are scored in the next category.

Chemicals causing mutagenic or genotoxic effects indirectly by interfering with various cellular systems would receive lower scores. Scores of two or four would be assigned to chemicals having positive evidence from certain test systems but clear evidence of lack of effects in other test systems.

It is assumed that all test data will be derived under optimal experimental conditions (e.g. using validated test procedures, including appropriate S-9 metabolic activating systems, adequately controlling for unusual chemical/physical characteristics of the test chemicals). Acceptable tests include, but are not necessarily limited to, the following:

a) in vitro gene mutation

- Salmonella/mammalian microsome assay
- CHO/HGPRT - assay
- L5178Y TK - assay
- Haploid Saccharomyces assay

b) in vitro mammalian chromosomal aberrations

- metaphase analysis in mammalian cells exposed in vitro
(not including sister chromatid exchange and micronuclei)

c) in vivo mammalian chromosomal aberrations

- rodent bone marrow micronucleus assay
- rodent bone marrow metaphase analysis
(not including sister chromatid exchange)

d) in vivo mammalian gene mutation or indicator tests in a second somatic tissue

- rodent liver unscheduled DNA synthesis
- rodent sister chromatid exchange

Data from other tests may be used with appropriate justification. There will be many chemicals for which adequate information for this element is lacking or incomplete. The use of structure-activity relationships in developing scores for this element may be a viable alternative in the future, however, at present such concepts are only in their formative stages (FDA, 1982; NTP, 1984; OSTP, 1985). Consequently, considerable expertise and judgment would be required to assign scores based on structure-activity information, and such scores would require appropriate modifiers to signify the level of confidence in the data used (e.g. !, ?, e).

The scoring criteria for this element are as follows:

ELEMENT SCORE	CRITERIA
10	Conclusive evidence of mutagenicity or genotoxicity in recognized prokaryotic or eukaryotic test systems at exposure levels not producing overt toxic effects.
8	Evidence of clastogenic effects (general DNA damage, strand breaks, sister chromatid exchange), intercalations or crosslinks but no evidence of increased incidences of mutations or direct interactions with genetic material.
6	Does not interact directly with DNA, but interferes with cellular mechanisms such as DNA synthesis and DNA repair. Effects may be observed at exposure levels associated with overt toxicity unrelated to genetic effects.
4	Mutagen/genotoxin in prokaryotic systems only (i.e. data from eukaryotic test systems are negative).
2	Mutagen/genotoxin in <u>in vitro</u> systems only (i.e. data from <u>in vivo</u> systems are negative).
0	No evidence of mutagenic or genotoxic effects in a adequate battery of test systems.

Suggested Information Sources

Information on the genotoxicity/mutagenicity of chemicals would generally be obtained from original publications and review articles as identified through MEDLINE, POLLUTION ABSTRACTS or TOXLINE databases or through the GenTox Information Service. Information may also be available from various summary data sources including Bowman, (1982), Fairchild (1978), Fishbein (1979), Ketchen et al., (1979), Kirsch-Volders (1983), Sax et al., (1981)-1986), Soderman (1983), Sontag (1982), and Stich (1984). It is difficult to judge the validity of genotoxicity/mutagenicity tests from summary data, however, and original publications should be consulted where possible.

P3E14 CARCINOGENICITY

Rationale

This element describes the potential of chemicals to cause cancer. Detailed assessment of the dose-response relationships, types of cancers produced, the validity of extrapolating carcinogenicity data among species and the processes of risk identification, assessment and management are beyond the sophistication of the scoring system and would form part of the final evaluation of chemicals assigned high priority by the system.

There is general agreement that radiation, biological, physical and chemical agents can cause cancer. In addition, the biochemical and molecular process of cancer development, as it is understood, is similar among mammalian species (NTP, 1984; OSTP, 1985). It is evident that the development of cancer is a multi-stage process involving interactions of agents with genetic material (the genome). The induction of a tumorigenic phenotypes through interactions with the genome may occur directly through the induction of somatic mutations or indirectly by alterations in gene expression. A number of factors affect the occurrence of these events, including age, sex, genetic differences, strain and species differences, diet, dose rate, route of exposure, interactions with other agents and a variety of environmental conditions (NTP, 1984; OSTP, 1985).

Furthermore, the production of these effects by a chemical may be by direct action of the chemical or its metabolites (e.g. direct acting, genotoxic carcinogens) or indirect through actions of the chemical on systems that secondarily produce tumorigenic phenotypes (e.g. non-genotoxic or epigenetic mechanisms). Although the detailed mechanism(s) of cancer production are not fully understood, it is evident that once the required modification in the genome occurs (known as initiation), the process is irreversible and self-propagating. A wide range of factors affect the initiation process, however, and many of these are believed to be reversible (IRLG, 1979; NTP, 1984; OSTP, 1985).

Although the exact mechanisms of the various stages of carcinogenesis are not fully understood, it is apparent that the events leading to the initiation of cells are dose-related (i.e. the frequency of occurrence of initiation increases with exposure). Once initiation has occurred, however, the subsequent development of tumours is independent of the exposure level (IRLG, 1979). This information is important to the scoring of the carcinogenic potential of a chemical.

Based on this brief summary of what is known about the process of carcinogenesis (refer to IRLG, 1979; NTP, 1984 and OSTP, 1985 for more detailed discussions), the scoring criteria for this element

differentiate between direct acting and indirect acting carcinogens. It is important that the scoring system not merely reflect the completeness of the data base (e.g. only a few chemicals have been adequately studied from an epidemiological point of view in human populations to assess their carcinogenicity). For many chemicals epidemiological studies to assess their carcinogenic potential will never be conducted and complete reliance will have to be placed in animal bioassay data for the evaluation of these chemicals. If the data from animal bioassays are viewed sufficiently strong, "epidemiologically proven" and "potential human" carcinogens (i.e. positive in animal bioassays) are given equal weight in the scoring system.

Scoring Criteria

The following definitions of carcinogenicity are used in scoring this element (Tomatis, 1979):

- Evidence of carcinogenicity is positive when an increase in malignant tumours is caused in more than one species or strain, in multiple experiments with varying routes or levels of exposure or to an unusual degree with respect to type, site, incidence or latency period.
- Evidence of carcinogenicity is negative when no tumour induction is observed in at least two adequate and appropriate animal studies in different species or in both animal and epidemiology studies.
- Evidence of carcinogenicity is inconclusive when neither of the above two conditions apply, usually because the observations are inadequate, of unacceptable quality or excessively limited. Contradictory results from different test systems may also lead to an inconclusive assessment. Such conditions are recorded as either positive or negative for carcinogenicity and tagged with either a ? or ! depending on the interpretation of the information by the scorer.

There is a great deal of controversy regarding the potency ranking of carcinogens, particularly when attempting to denote the potency of a chemical to cause cancer in man from data derived from animal cancer bioassays. Animal bioassays utilize high exposure levels (known as the Maximum Tolerated Dose or MTD protocol, see NTP, 1984; OSTP, 1985). Judgments of carcinogenic potency based on information derived from such high levels of exposure may have little relationship to potencies at lower levels of exposure comparable to those found in the environment. Consequently, the basis for potency ranking is not considered adequately developed for use in a scoring system, however, if procedures for such ranking were found reliable, they would form a reasonable basis for the scoring of the carcinogenic potential of chemicals.

Important information to assist in the interpretation of animal cancer bioassay data vis-a-vis the potential of a chemical to cause cancer in humans can be derived from assessments of its mutagenicity/genotoxicity (considered in element P3E13).

Since the International Agency for Research on Cancer (IARC, 1980b; 1983) conducts expert reviews and assessments of the potential carcinogenic risks of chemicals to humans, this data base will be a prime source of information for scoring element P3E14. Consequently, the relationship between the IARC system for assessment of evidence of carcinogenicity and the scoring criteria summarized below must be clarified. The IARC (1980b) classifies their assessment of carcinogens into one of five groups.

a) Sufficient Evidence of Carcinogenicity

This classification requires adequate evidence of increased incidence of malignant tumours in multiple species or strains, or in multiple experiments (preferably with different routes of administration and using different dose levels), or to an unusual degree with respect to incidence, site, type of tumour or age of onset. Additional evidence used is derived from information on dose-response relationships, mutagenicity/genotoxicity or chemical structure.

This classification also applies to cases where a causal association has been established between the chemical and human cancer.

b) Limited Evidence of Carcinogenicity

This classification requires data suggesting a carcinogenic effect, but are limited due to studies on a single species, strain or experiment; factors restricting the interpretation of the data (e.g. inadequate dose levels, duration of exposure, period of exposure or follow-up, poor survival, too few animals or inadequate reporting; or the neoplasms produced often occur spontaneously, or are difficult to classify by histological criteria alone).

If epidemiological data are available, this classification would indicate a possible carcinogenic effect in humans, but the data available are not sufficient to demonstrate a causal relationship.

c) Inadequate Evidence of Carcinogenicity

This classification is based on major qualitative or quantitative limitations in the data, thus limiting the interpretation of the presence or absence of a carcinogenic effect in laboratory animals or human populations.

d) Negative Evidence of Carcinogenicity

The chemical is not carcinogenic, within the limits of the tests used.

e) No Data Available.

Generally, substances classified by IARC as "Sufficient Evidence" of carcinogenicity could be scored between 2 and 10 according to the criteria outlined below. "Limited evidence" of carcinogenicity would be signified by the addition of a ! modifier of the score assigned. "Inadequate Evidence" would be scored with a ? modifier. "No Data Available" would be signified with an * modifier. "Negative Evidence" would be scored 0.

The scoring scheme for element P3E14 is as follows:

ELEMENT SCORE	CRITERIA
10	Direct acting human carcinogen or potential human carcinogen (based on animal bioassay data) with evidence of direct interactions with genetic material. Acts as an electrophile or direct alkylating agent, produces DNA adducts, induces cell transformation, etc.
8	Indirect acting human carcinogen or potential human carcinogen (based on animal bioassay data) with evidence that it does not interact with genetic material.
6	Tumourigenic in animal bioassay tests at levels of exposure shown to saturate enzymes involved in the metabolism of the compound OR at exposure levels shown to cause histopathological lesions known to predispose animals to the development of cancers at sites where the lesions are observed (e.g. ATPase deficient liver foci in rodents). Adequate evidence must be available demonstrating that no interactions occur with genetic material and that the chemical does not induce cell transformation.
4	Positive tumorigenic agent (benign tumors) in humans or animals. Evidence must be available of lack of interactions with genetic material. Includes chemicals that act solely as promoters and those that cause cell transformation <u>in vitro</u> without evidence in other systems.
2	Tumorigenic in only one animal species and negative in other(s) (all studies considered adequate).
0	Not tumorigenic in adequate studies and must not interact with genetic material.

Information Sources

Information on the carcinogenicity of chemicals would generally be obtained from original publications and review articles as identified through IARC Monographs or MEDLINE, POLLUTION ABSTRACTS, TOXLINE databases or National Toxicology Program (NTP) publications. Information may also be available from various summary data sources including Bowman, (1982), Fairchild (1978), Fishbein (1979), Ketchen *et al.*, (1979), Kirsch-Volders (1983), Sax *et al.*, (1981-1986), Söderman (1983), Sontag (1982), and Stich (1984). However, it is difficult to judge the validity of carcinogenicity data from summary data and original publications

should be consulted.

P3E15 UNDESIRABLE AESTHETIC PROPERTIES

Rationale

The undesirable aesthetic properties of chemicals were scored in Phase 2, element P2E9 based on the concentrations in water or air that produced the unwanted effects. Element P3E15 retains the P2E9 score such that chemicals with undesirable aesthetic properties are identified when visualizing the Phase 3 vector.

Scoring Criteria

The scores assigned to Element P2E9 of the Phase 2 vector are transferred to P3E15. Element P2E9 criteria are as follows:

ELEMENT SCORE	CRITERIA	
	Water Related Effects	Air Related Effects
3	Occur at <0.01 mg/L	Occur at <0.01 ppm
2	Occur at 0.01-10 mg/L	Occur at 0.01-10 ppm
1	Occur at >10 mg/L	Occur at >10 ppm
0	Not known to occur	Not known to occur

Suggested Information Sources

Scores for Element P3E15 are obtained from Element P2E9 of the Phase 2 vector.

7.0 COMBINING RULES FOR PHASE 3 ELEMENTS

7.1 General Considerations

The general philosophy of the combining rules for the elements of the Phase 3 vector is similar to that used in Phase 2. The magnitude of the element score expresses the level of concern associated with the property of a chemical represented by that element. Combining rules are applied to the elements of the vector to establish the level of priority a chemical should receive for detailed evaluation in the regulatory process.

For the purpose of simplifying the description of Phase 3 combining rules, the elements of the vector are discussed using two groupings:

Exposure elements = P3E1 through P3E7 ("E" elements)

Toxicity elements = P3E8 through P3E14 ("T" elements)

The following general principles have been considered in developing the combining rules used for Phase 3:

- a) Combining rules are used to assign chemicals to priority lists. Some combining rules consider only one element, which, if the score is sufficiently high, can justify placement of the substance on the highest priority list (i.e. list 1). Other rules consider combinations of element scores. Maximum or minimum limits are applied to the combinations to determine on which lists chemicals are placed.

Lists of chemicals should also retain all their element scores and score modifiers for the Phase 3 vector. This procedure ensures that the information available on the chemicals is retained and can be used in subsequent decisions on the prioritization of chemicals for detailed regulatory consideration.

- b) Chemicals on List 1 (P3L1) would be considered of highest priority for regulatory evaluation. Others include List 2 (P3L2; medium priority), List 3 (P3L3; low priority), List 4 (P3L4; Undesirable Aesthetic Properties) and List 5 (P3L5; Inadequate Information).
- c) Priority ranking within lists may be accomplished in two ways. First, the Phase 3 vectors for chemicals within a list can be assessed visually since each vector represents a "finger-print" of the element scores for a chemical. With this approach, chemicals with unusual characteristics are readily identified and assigned priorities depending on the focus required (e.g. chemicals with high toxicity scores but insufficient information in the exposure elements to enable

detailed assessment may be place on special lists for information gathering).

The second method of priority ranking within lists is based on the sum of all elements for chemicals on that list. Since all lists, except number one, group chemicals with comparable data bases, these procedures combine scores of chemicals for which roughly comparable levels of data are available. Numerical ranking may be conducted first, followed by ad hoc visual assessment of the vector elements to identify any inconsistencies or problems that may lead to difficulties in detailed regulatory assessment. Specific actions could then be taken to address identified difficulties prior to detailed assessment.

- d) The presence of a sufficient number of asterisks (signifying inadequate information) to prevent the summation of two scores from the "E" or "T" classes of elements results in placement of the chemical on the inadequate information list.
- e) As in the combining rules for the Phase 2 vector elements, when chemicals are assigned to priority lists, they are accompanied by all their vector elements including assigned scores and modifiers. This ensures retention of all the information used in scoring the chemical and allows sorting within lists and identification of factors critical to the prioritization of the chemical.

7.2 Specific Combining Rules for Phase 3

The combining rules for the elements of the Phase 3 vector are listed below are also summarized in Figure 2.

P3R1 If any of the toxicity ("T") elements score eight (8) or greater, and the highest score of any of the "E" elements is greater than zero, place the chemical on P3L1. If this criterion is not met, pass the chemical to P3R2.

This rule ensures that chemicals with high toxicity and some potential for exposure receive high priority for regulatory assessment.

P3R2 If the chemicals has six or more asterisks (*) in either the "E" or "T" elements (i.e. scores cannot be assigned for these elements), place is on P3L5 (inadequate information). If not, pass it to rule P3R3.

This rule ensures that all chemicals lacking adequate information for scoring are listed separately.

P3R3 If the sum of the two highest scoring elements in the "E" and "T" groups is equal to or greater than 24, place the chemical on List 1 (P3L1). If not, pass the chemical to P3R4.

This rule ensures that chemicals with moderate toxicity but high exposure are on the highest priority list for regulatory consideration.

P3R4 If the sum of the two highest scoring elements in the "E" and "T" groups is equal to or greater than 14, place the chemical on List 2 (P3L2). If not, pass the chemical to P3L3.

This rule ensures that chemicals with moderate toxicity and moderate exposure are on the medium priority list (P3L2).

P3R5 Subtract all chemicals considered for regulatory assessment from the chemicals on P2L4 (Undesirable Aesthetic Properties List from Phase 2). Enter those chemicals remaining on List P3L4. These are the chemicals with undesirable aesthetic properties which will not receive regulatory assessment following Phase 3 prioritization. The requirement for regulation of these chemicals can then be assessed, independent of their toxicological properties.

7.3 Selection of Chemicals from Phase 3 Lists for Detailed Regulatory Assessment

Generally, chemicals would be selected for detailed regulatory consideration based on the ranking within Lists 1 and 2. In all cases, element modifiers (?, !, e) will be evaluated on an ad hoc basis after ranking of chemicals within a list but before final assessment. The impact of the element modifiers on the sum of the element scores will require judgment by the user of the scoring system. This assessment will help reduce the impact of compounding worst-case data estimates or questionable data on the final selection of a chemical for regulatory consideration.

The selection of chemicals for detailed regulatory consideration is based on the following steps:

- a) Chemicals from P3L1 receive highest priority. P3L1 identifies chemicals with high levels of toxicity. Highly toxic chemicals appear on P3L1 even though they may have low exposure potential or substantial numbers of asterisks (*) in other elements. The impact of such information would be evaluated during detailed regulatory assessment.

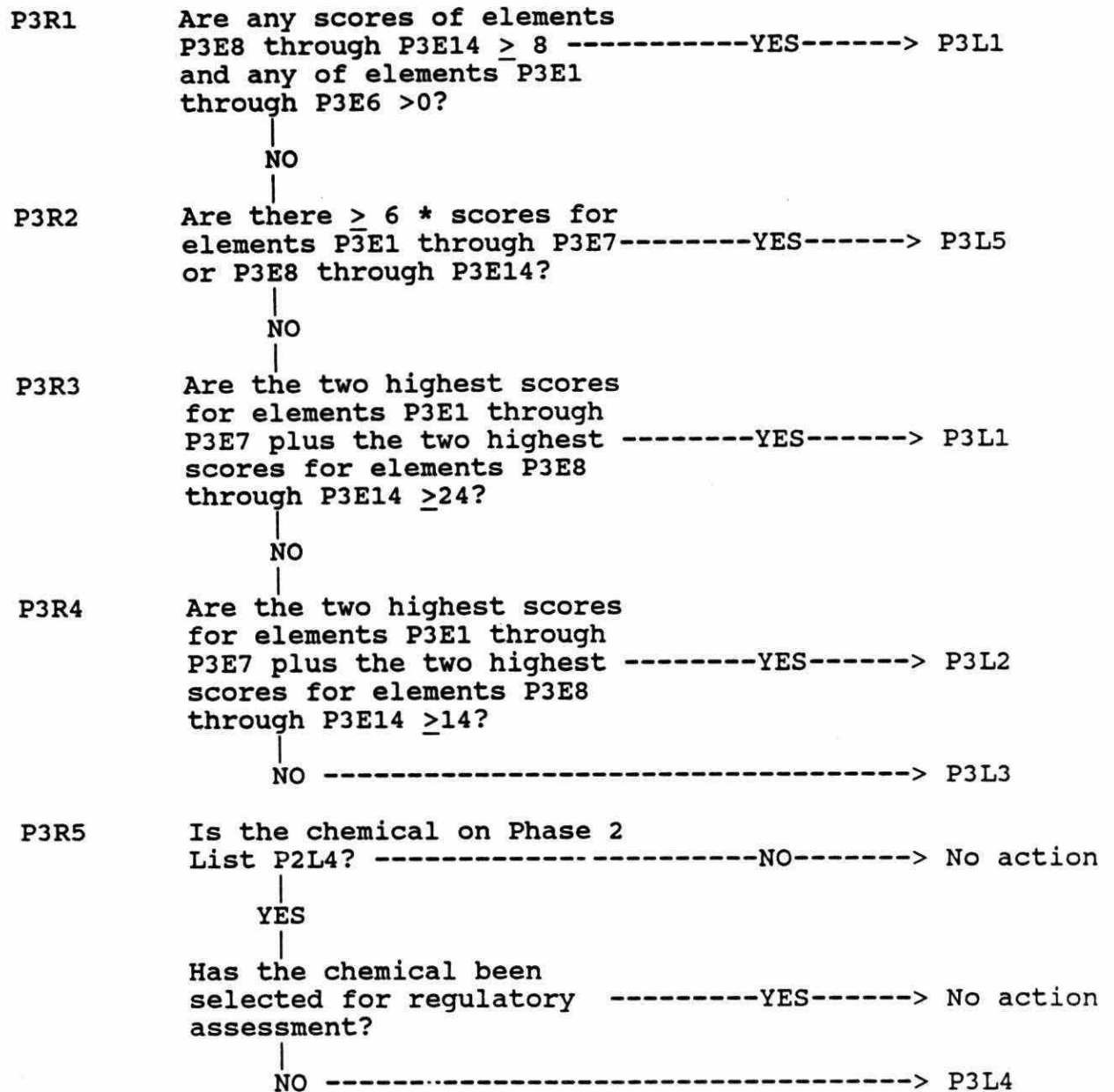
During the process of regulatory assessment, scores for environmental concentrations and dispersion characteristics would be evaluated. If adequate information is not available to score the elements describing parameters important in assessing exposure potential, such data will have to be acquired as part of the regulation-setting process. The importance of these issues to the selection of the chemical will be based on the judgment of the user.

Chemicals with moderate toxicity and high exposure will also receive the highest priority for regulatory assessment.

- b) Chemicals on P3L2 are ranked in priority according to either the sum of their element scores or ad hoc visual assessment of the Phase 3 vectors, or a combination of both approaches. These chemicals would be generally considered for detailed regulatory assessment after those on P3L1, unless ad hoc assessment of the vector highlights special concerns. P3L2 identifies chemicals with lower toxicity and exposure scores than those in P3L1, therefore they receive lower priority.
- c) Chemicals on P3L3 are ranked lowest in priority for regulatory consideration.
- d) Chemicals on P3L4 are those with undesirable aesthetic properties that have not been given regulatory consideration based on exposure and toxicological parameters. These chemicals would be assessed on an ad hoc basis.
- e) Chemicals on P3L5 lack adequate information of prioritization. In order to identify all chemicals passed through the scoring system with inadequate information, P2L5 and P3L5 are combined.

Assessment of this list would provide valuable information for data gathering exercises. Priorities for data gathering may be established by ad hoc visual assessment of the vectors for these chemicals. As missing data is collected, these chemicals could be scored appropriately.

FIGURE 2 Flow Diagram for Phase 3 Combining Rules



8.0 SEARCH STRATEGY

8.1 Phase 2 Search Strategy

The elements in Phase 2 were developed to minimize the need to search extensively through the primary literature sources. As a result a premium is placed on reviews and compilations of information. For example, physical and chemical properties for many substances are listed in relatively well-known sources such as the Merck Index, the Condensed Chemical Dictionary (Hawley, 1977), the Handbook of Environmental Data on Organic Chemicals (Verscheuren, 1983), and the Handbook of Estimating Physicochemical Properties (Lyman *et al.*, 1982). Similarly, reviews of health considerations such as those found in monographs prepared by IARC and Patty's Industrial Hygiene Publications (Clayton and Clayton, 1981) are the types of sources well-suited for use in Phase 2.

A second valuable source of information in Phase 2 are databases that provide actual data instead of citations alone. Examples suggested for various Phase 2 elements include ENVIROFATE, ISHOW, TSCAPP, RTECS and there are many others. Many of these offer the option of searching according to Chemical Abstract Service (CAS) number which makes searching efficient and relevant. While the results from database searches often identify original sources, these sources would not need to be consulted for Phase 2.

A third source of Phase 2 data includes reports prepared by various regulatory and advisory agencies. Examples include those prepared by the Associate Committee on Environmental Quality of the National Research Council of Canada, ambient water and health assessment documents prepared by the U.S. Environmental Protection Agency, and the environmental health criteria publications of the World Health Organization.

Many sources of information are identified following the descriptions of each Phase 2 element in addition to those already noted. These tend to be recent reports or journal articles that provide information about wide ranges of substances or can provide guidance to those responsible for assigning scores. It is inevitable that in time similar or improved sources will become available. Accordingly, the lists of sources should not be perceived as being comprehensive or static but rather represent some of the appropriate sources that are currently available.

Table 8.1 is a summary of the suggested information sources for the Phase 2 elements.

TABLE 8.1 Summary of Data Sources for Phase 2 (Listed Alphabetically)

Source Name	Phase 2 Element Number									Comments
	E1	E2	E3	E4	E5	E6	E7	E8	E9	
AQUIRE Database						X	X	X		Contains BCF data.
Clayton and Clayton (1981)							X	X		Summarizes toxic characteristics of a number of industrial chemicals, primarily in terrestrial species.
ENVIROFATE Database				X	X					Contains solubility, biodegradability, vapour pressure, partition co-efficients.
Hayes (1982)							X	X		Information on toxicology of pesticides
ICF Inc. 1985				X	X	X				Contains tabulations of physical, chemical and fate data for many organic substances.
Ketchen <i>et al.</i> , (1979)	X	X		X	X					Data sheets containing information on the toxic potential of individual chemicals includes acute lethality data.
Lyman <i>et al.</i> , (1982)				X		X				A review of published values and estimation methods for various physical and chemical properties.
MERCK Index							X	X		Lists toxicity for many chemicals in terrestrial species.
Mills <i>et al.</i> , (1982)							X	X		Compilation of physical, chemical and fate data for many organic substances.
MOE Industrial Survey, 1981		X		X						Provides information on industrial chemicals used in Ontario.

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TABLE 8.1 Summary of Data Sources for Phase 2 (Listed Alphabetically)

Source Name	Phase 2 Element Number									Comments
	E1	E2	E3	E4	E5	E6	E7	E8	E9	
RTECS Database						X	X	X		Contains LD ₅₀ and LC ₅₀ values for a variety of terrestrial and aquatic plus any positive results indicating systemic toxicity, Provides emission rates and environmental levels for industrial chemicals.
US Environmental Protection Agency 1977		X	X							
Verschueren (1983)				X	X		X	X	X	

8.2 Phase 3 Search Strategy

Unlike Phase 2 where the emphasis is on gathering information quickly, Phase 3 requires a more carefully planned and intensive information search strategy. This strategy will be largely substance-specific and therefore cannot be spelled out in the detail of the Phase 2 searches.

Phase 3 searches will require more collecting of original articles (as opposed to reviews). Articles to be sought can include those listed in the bibliographies of reviews or identified as sources in factual database citations.

Bibliographic databases can be a major source of original articles to be collected. Examples of such databases include BIOSIS, NTIS, Chemical Abstracts, Toxline, and Medline. How a search proceeds will depend upon the articles identified, the availability of materials, the time and care taken, and the skill of the investigator.

Several of the Phase 3 elements require the results of monitoring surveys or estimates of environmental concentrations. The procedures for the estimation of environmental concentrations are addressed in Appendix D. Most monitoring is undertaken by provincial or federal agencies. In addition to information compiled by the MOE and Environment Canada, data for a specific substance or environmental compartment may have been gathered by other Ontario ministries such as Agriculture and Food, Natural Resources, Health and Labour. Increased environmental awareness and the undertaking of studies such as environmental impact assessments may also result in private industries, conservation authorities, utilities and special government agencies collecting environmental data in specific areas or about specific chemicals. If Ontario data are scarce or absent, U.S. data should be consulted (e.g. data collected in nearby states or by the U.S. EPA).

Table 8.2 is a summary of the suggested information sources for the Phase 3 elements. The sources listed illustrate locations of useful data but investigative skills will be a major factor in Phase 3 searches for information.

Due to the lag-time needed for the entry of published scientific information onto various databases, there is a need to "hand-search" recent scientific publications to cover this gap in the information available on computer-accessed data bases. Experience indicates that searching various scientific journals over the latest 6 months is adequate to ensure all available published information is considered in developing element scores in Phase 3. Table 8.3 lists a number of scientific journals that should be included in such hand-searches. The list of journals included should be periodically up-dated to include new scientific journals that are published.

TABLE 8.2 Summary of Data Sources for Phase 3 (Listed Alphabetically)

Source Name	P2	E1	E2	E3	E4	E5	E6	E7	E8	E9	E10	E11	E12	E13	E14	E15	Comments
AQUIRE Database													X	X	X		Contains BCF Data.
Clayton and Clayton (1981)										X			X	X			Summary of toxic characteristics of a large number of industrial chemicals, primarily in terrestrial species.
Environment Canada Monitoring Data		X	X	X	X	X	X	X									Monitoring data on air, water and soil quality.
Ketchen <u>et al.</u> , (1979)		X								X			X	X	X		Critical material data sheets containing information on the toxic potential of acute lethality data in terrestrial species.
MEDLINE Database										X			X	X	X	X	Presents titles, abstracts of published worldwide literature.
MERCK Index										X			X				Indices of toxicity for many chemicals in terrestrial species.
Ministry of Natural Resources												X					Provides wildlife toxicity data.
MOE Monitoring Data		X	X	X	X	X	X	X									Criteria reviews and monitoring data on air, water, and soil quality.
PHYTOTOX												X					Contains plant toxicity data.
TOXLINE Database													X	X	X	X	Contains citations of original research and reviews in the general field of toxicology.
US Environmental Protection Agency		X	X			X	X		X								Provides emission rates for various industrial activities.
US FDA Monitoring Data						X	X		X								Data on contaminants in foods.

TABLE 8.3 LIST OF SUGGESTED SCIENTIFIC JOURNALS FOR
"CURRENT" INFORMATION SEARCH FOR PHASE 3

Amer. J. Path.	Environ. Mutagenesis
Anal. Chem.	Environ. Res.
ACTA Pharmacol. Toxicol.	Environ. Toxicol Chem.
ACTA Physiol. Acad. Sci.	Europ. J. Toxic Environ. Hyg.
Air Water Soil Poll.	Exp. Mol. Path.
Arch. Environ. Contam. Toxicol.	Food Cosmet. Toxicol.
Arch. Environ. Health	Fund. Appl. Toxicol.
Arch. Pharmacol.	Gann
Arch. Toxicol.	Genetics
Atmospheric Res.	Gig. Sanit.
Biochem. Pharmacol.	Histopath.
Bull. Environ. Contam. Toxicol.	Int. Arch. All. Appl. Immunol.
Brit. J. Ind. Med.	Int. Arch. Occ. Env. Health
Brit. J. Cancer	Int. J. Cancer
Brit. J. Exp. Path.	J. Analytical Toxicol.
Clin. Chim. ACTA	J. Chem. Eng. Data
Can. J. Fish. Aquat. Sci.	J. Environ. Health
Can. Vet. J.	J. Environ. Path. Toxicol.
Cancer Chemother. Reports	J. Environ. Sci. Health
Cancer Lett.	J. Hazardous Materials
Cancer Res.	J. Nat. Cancer Inst.
Carcinogenesis	J. Pharmacol. Exp. Therapeut.
Chemosphere	J. Phys. Chem. Ref. Data
Clin. Res.	J. Toxicol. Environ. Health
Clin. Toxicol.	J. Toxicol. Sci.
Comments on Toxicology	J. Water Poll. Control Fed.
Drug Chem. Toxicol.	Marine Poll. Bull.
Dang. Prop. of Ind. Mat. (Sax)	Mutat. Res.
Environ. Sci. Toxicol.	Nature
Ecotoxicol. Environ. Safety	Neurotoxicol.
Environ. Health Perspect.	Regulatory Toxicol. Pharmacol.

TABLE 8.3 LIST OF SUGGESTED SCIENTIFIC JOURNALS FOR
"CURRENT" INFORMATION SEARCH FOR PHASE 3

Teratology
Toxicol. Appl. Pharmacol.
Science
Toxicol. Lett.
Toxicology
Toxicol. Europ. Res.
Vet. Human Toxicol.
Water Res.

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APPENDIX A - SUMMARY OF PREVIOUSLY DESCRIBED SCORING SYSTEMS

A1.0 Summary of Previously Described Scoring Systems

Screening systems have become a useful tool in the hazard assessment of chemicals for the purpose of assigning priority for regulation or further testing. Several screening systems have been developed which base the assessment on various different parameters related to the biological effects, exposure potential and/or environmental fate of the chemical.

A recently published review by Hushon and Kornreich (1984) discusses 34 different screening systems. The authors deal with factors to be considered in screening system design or selection, steps involved in scoring and criteria used for scoring. They emphasize that when selecting or designing a scoring system, the specific purpose of the program must be clearly defined and the system tailored to satisfy the particular requirements of the program. The scoring system must not ignore missing data. If data are not readily available then scoring criteria may have to be redefined, or missing data may have to be estimated based on modelling, data from QSAR studies, average values or worst-case values. The role of expert judgement and the possibility of bias towards high scores for chemicals which have been studied in great detail must be considered as well as the needs of the program and the availability of data. The first step involved in the scoring process involves selecting the group of chemicals which will be considered. This list usually will need to be reduced by some crude screening procedure to generate a group of chemicals of specific interest which can be examined in more detail. This list may be further divided if desired by grouping chemicals according to physio-chemical properties or chemical structure. Data collection must be as thorough as possible, but compromises usually have to be made between completeness and efficiency. Scoring is usually accomplished by allowing the scorer a choice of statements which describe each parameter upon which the overall score will be based. The statements are numerically graded based on extent of contribution to hazard potential and the scorer chooses the appropriate statement and assigns the designated score. Scores may be combined to reach an overall score or scores from various elements (e.g., environmental fate, exposure or toxicity) may be grouped together to give scores for individual elements. Scores may be combined additively, multiplicatively or not at all. Scores may be combined as they are or they may be weighted according to the nature of the data and the requirements of the program. The criteria used for scoring are determined based on the available data and the needs of the program. For assessment of exposure, the criteria used may be production of the chemical, use, release, environmental fate, size and type of population at risk and dose. The assessment of biological effects may involve the use of criteria such as metabolism and pharmacokinetics, acute toxicity, chronic toxicity, carcinogenicity, mutagenicity, teratogenicity and reproductive effects. The assessment of environmental effects may require consideration of lethality, growth and development,

reproduction, bioaccumulation and other toxic effects of the chemical on microbes, algae, plants, invertebrates, fish, birds and mammals.

The 34 screening systems discussed by Hushon and Kronreich are classified by type and their scoring capabilities compared. A summary of the scoring systems discussed is shown in Table 1. The reader is referred to this source for a comprehensive discussion of screening system design and scoring. For a discussion of methods used to screen carcinogens and rank them for potency based on epidemiology, lifetime bioassays, animal skin painting, short-term tests, acute toxicity and structure-activity relationships, the reader is referred to a review by Barr (1985).

In this appendix, two screening systems will be discussed which were not dealt with by Hushon and Kornreich (1984). The first is a ranking system for environmental assessment (Klein et al., 1984) and the second is a comprehensive hazard evaluation system developed for EPA/OTS by ORNL (O'Bryan, 1986).

The screening system described by Klein, et al., (1984) is designed to rank chemicals for environmental assessment based on environmental hazard profiles. The profile contains bioconcentration factors in algae, fish and activated sludge, retention time in rats, biodegradation rate in activated sludge, photomineralization rate and extent of toxicity to Daphnia. Based on the values in the profile, chemicals are scored as: I. having a low likelihood of presenting an environmental hazard; II. having an uncertain (or medium) likelihood of presenting an environmental hazard; or III. having a high likelihood of presenting an environmental hazard. Seven different ways of weighting the seven parameters used for the assessment were compared for a group of 15 chemicals. Most of the chemicals fell into category II regardless of the weighting system used. This method of comparing results using different weighting systems increases the level of certainty of the correctness of the classification, but only if the level of certainty does not change with different weightings of parameters (Klein et al., 1984).

The screening system described by O'Bryan (1986) is a modified and refined version of a system developed in 1981 for EPA/Office of Toxic Substances by Oak Ridge National Laboratories (Ross and Lu, 1981) and reviewed by Hushon and Kornreich (1984). This is a comprehensive hazard evaluation system by which chemicals are scored for oncogenicity, genotoxicity, developmental toxicity, acute and chronic mammalian toxicity, aquatic toxicity, bioconcentration, production volume, occupational exposure, consumer exposure, environmental exposure and environmental fate. Each parameter is scored independently and the scores are not combined or weighted in any way. Expert scorers use objective guidelines and professional judgement to reach a score. Scorers provide rationale for the scores they assign. Two independent

scorers score each chemical and they discuss their ratings if they are in disagreement. If no agreement can be reached then both scores are used. This system is designed for rapid evaluation with readily available information.

A2.0 Table I: Screening Systems Discussed
by Hushon and Kornreich

Title	Purpose	No of Subst's	References
Pesticide Manufacturing Air Prioritization	to characterize air-borne exposure to organic pesticides	80	Archer <u>et al.</u> , (1978)
Sequential Testing for Toxicity Classification	to rank toxicity of a new chemical by a variety of routes and test systems	500	Astill <u>et al.</u> , (1980)
Index of Exposure	to indicate relative potential for exposure associated with a given use of each chemical		Auerbach Associates Inc. (1977)
Chemical Hazard Ranking System	to rank chemical components of consumer products by probable health impact		Becker, (1978)
System for Evaluation of Bulk Water Transportation of Industrial Chemicals	to identify hazards of chemicals being transported by water		Beckmann (1974)
Barring Model	to rank dumpsite chemicals as hazardous or safe		Booz-Allen Applied Research, Inc. (1975)
Select Organic Compounds Hazardous to the Environment	to identify high exposure compounds for review by NSF panel concerning damage to health or environment	337	Brown <u>et al.</u> (1975)
Ranking Algorithm for CEL Water Pollutants	to select chemicals in aquatic environment for further study	1500	Brown <u>et al.</u> (1980)
Setting Priorities for Research and Development on Army Chemicals	to select research priorities	35	Brown <u>et al.</u> (1978)

Title	Purpose	No of Subst's	References
System for Rapid Ranking of Environmental Pollutants	to choose chemicals on which to prepare scientific and technical reports	10	Brown <u>et al</u> (1976)
Estimating the Hazard of Chemical Substances to Aquatic Life	to determine impact of chemicals on aquatic life		Cairns <u>et al</u> (1979)
Estimation of Toxic Hazard - A Decision Tree Approach	to identify potentially dangerous food constituents for further testing	247	Cramer <u>et al</u> (1978)
TSCA-ITC Scoring Scoring Workshop	to develop an improved health and environmental effects scoring system to identify chemicals for further testing	6	Enviro Control Inc.(1979)
An Approach to Prioritization of Environmental Pollutants: The Action Alert System	to help the OWRS to set priorities regarding chemicals indentified in water	129	Fiksel and Segal (1982)
Scoring of Organic Air Pollutants	to select organic air pollutants for further study/monitoring	637	Fuller <u>et al</u> (1976)
Ranking of Environmental Contaminants for Bioassay	to select chemicals for NCA bioassay		Gori(1977)
PHL Model	to identify landfill components likely to represent human health hazards		Hagerty <u>et al.</u> , (1973)
Hazard Evaluation Procedure for Potentially Toxic Chemicals	screening procedure to identify high-risk chemicals		Harriss (1976)

Title	Purpose	No of Subst's	References
Selection of Chemicals for Inclusion in a Trend Monitoring	to select chemicals and chemical classes to include in a monitoring program to follow trends	700	Hushon <u>et al</u> (1978)
RCRA Risk/Cost Policy Model	to identify relative risks from exposure to chemicals in wastes	140	ICF Inc. (1982)
ITC Scoring for Biological Effects		317	Interagency Testing Committee (1977)
Ranking of Food Contaminants	to identify for OTA organics, inorganics and radionuclides that are possible food contaminants	143	Kornreich (1979)
Rapid Screening and Identification of Airborne Carcinogens of Greatest Concern		47	Margler <u>et al</u> (1979)
Critical Materials Register	to construct a register of chemicals of concern	178	Michigan Dept. of Natural Resources (1979)
National Occupational Hazard Survey	to rank hazards according to the amount of occupational exposure	7145	NIOSH (1977)
Assessment of Oncogenic Potential	to identify carcinogens and to rank them relative to the evidence		Nees (1979)
ITC Scoring for Exposure	to rank chemicals on the basis for potential human exposure and environmental release	1834	OTS/EPA (1978)

Title	Purpose	No of Subst's	References
Ordering of Commercial Chemicals on NIOSH's suspected Carcinogens List	to determine which suspected carcinogens are of concern to OPTS	1768	OTS/EPA (1978)
Identification of High Risk Occupational Groups and Industrial Processes Using RTECS/NOHS Data	tool to objectively assess potential health risk from workplace exposure	28,000	Pielmeier (1981)
OECD Ecotoxicology Testing Scheme	to test how well aquatic tests predict hazard potential (1980)	53	Pommeroy <u>et al.</u> ,
Chemical Scoring System Development	to select chemicals for more in depth evaluation by OPTS	6	Ross and Lu (1981)
Environmental Scoring of Chemicals	to select chemicals presenting environmental risk under TSCA and for use by ITC to identify chemicals for further environmental testing	10	Ross and Welch (1980)
Ranking Animal Carcinogens	to classify animal carcinogens to permit the use of regulatory options	10	Squire (1981)
Hazard Assessment by a Qualitative System	to determine whether a new chemical represents a hazard based on MPD data	47	Jouany <u>et al</u> (1982)

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From: Hushon and Kornreich (1984)

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APPENDIX B - SCORING CRITERIA FOR PHASE 2 AND PHASE 3 VECTOR
ELEMENTS

TABLE B-1

SCORING CRITERIA FOR PHASE 2 VECTOR ELEMENTS

ELEMENT NUMBER	UNITS	SCORING CRITERIA			
		0	1	2	3
P2E1	kg/yr	<5	5 to 300	300 to 10000	>10000
P2E2	% release narrative	0 not used or imported in Ontario	0 to 3 used in closed systems with no routine releases	>3 to 30 Most converted to another product, OR OR largely restricted to industrial uses, OR very slowly released, OR shipped in large batches	>30 Most released directly into the environment, OR used in an open, dispersive manner
P2E3	Measurement basis	No yet detected in Ontario	Infrequently detected at specific locations	Frequently detected but only at specific sites	Frequently detected over much of Ontario
	Release basis	No known release sites in Ontario	Few release sites concentrated in a few locations	Relatively few release sites, but not concentrated in a few locations	Many release sites throughout Ontario
P2E4	narrative	<5% of releases partitions into other media, OR vapour pressure ≤ 1 kPa, solubility ≤ 100 g/m ³	\geq one media other than receiving medium containing 5-10% of the amount released, OR vapour pressure ≤ 1 kPa, solubility ≤ 100 g/m ³	\geq one media other than receiving medium containing 10-20% of the amount released, OR vapour pressure > 1 kPa, solubility > 100 g/m ³	> two media other than receiving medium containing more than 20% of the amount released, OR vapour pressure > 1 kPa, solubility > 100 g/m ³ , OR most is associated with fine particles when released into the environment
P2E5	t 1/2 (days) narrative	<10 designated not persistent	10 to <50 slightly persistent	50 to <100 moderately persistent	>100 very persistent
P2E6	BCF Log K _{ow}	≤ 20 ≤ 2.0	>20 to 500 >2.0 to 4.0	500 to 15000 >4.0 to 6.0	>15000 >6.0
P2E7	Oral LD ₅₀ mg/kg	>5000	>500 to 5000	50 to 500	<50
	Dermal LD ₅₀ mg/kg	>5000	>500 to 5000	50 to 500	<50
	Inh LC ₅₀ mg/m ³	>15000	>1500 to 15000	150 to 1500	<150
	Aquatic LC ₅₀ mg/L	>1000	>100 to 1000	10 to 100	<10

TABLE B-1 SCORING CRITERIA FOR PHASE 2 VECTOR ELEMENTS

ELEMENT NUMBER	UNITS	SCORING CRITERIA			
		0	1	2	3
P2E8	Narrative	No evidence of chronic effects in more than one species	Evidence of chronic effects not detrimental to the continued development and well-being of the test system	Evidence of chronic adverse effects in one species but negative data in another species	Evidence of chronic effects in more than one species
P2E9	water mg/L	No effects	>10	0.01 to 10	<0.01
	air ppm	No effects	>10	0.01 to 10	<0.01

TABLE B-2 SCORING CRITERIA FOR PHASE 3 VECTOR ELEMENTS

ELEMENT NUMBER ^a	Units	0	2	4	6	8	10
P3E1	ug/M ³	<0.03	>0.03-0.3	>0.3-3	>3-30	>30-300	>300
P3E2	ug/L	<0.3	>0.3-3	>3-30	>30-300	>300-3000	>300
P3E3	ug/kg with						
	K _{OW} <1	<0.6	≥0.6-6	>6-60	>60-600	>600-6000	>6000
	K _{OW} 1-3	<6	≥6-60	>60-600	>600-6000	>6000-60000	>60000
	K _{OW} 3-5	<60	≥60-600	>600-6000	>6000-60000	>60000-600000	>600000
	K _{OW} >5	>600	≥600-6000	>6000-60000	>60000-600000	>600000-6000000	>6000000
P3E4	ug/kg	>5	≥5-50	>50-500	>500-5000	>5000-50000	>50000
P3E5	ug/kg	<0.6	≥0.6-6	>6-60	>60-600	>600-6000	>6000
P3E6	ug/kg	<0.6	≥0.6-6	>6-60	>60-600	>600-6000	>6000
P3E7	release-	<1	≥1-10	>10-50	>50-150	>150-300	>300

TABLE B-2 SCORING CRITERIA FOR PHASE 3 VECTOR ELEMENTS

ELEMENT NUMBER	Units	0	2	4	6	8	10
P3E8	oral LD ₅₀ mg/kg	>5000	>500-5000	>50-500	>5-50	>0.5-5	≤0.5
	dermal LD ₅₀ mg/kg	>5000	>500-5000	>50-500	>5-50	>0.5-5	≤0.5
	inhalation LC ₅₀ mg/m ³	>15000	>1500-15000	>150-1500	>15-150	>1.5-15	≤1.5
	aquatic LC ₅₀ mg/L	>1000	>100-1000	>10-100	>1-10	>0.1-1	≤0.1
P3E9	aquatic non-mammals - EC ₅₀ , mg/L	≥20	>20-2	>2-0.2	>0.2-0.02	≤0.02	≤0.02
	MATC, mg/L	≥2	>2-0.2	>0.2-2	>0.02-0.002	≤0.002	≤0.002
	NOAEC, mg/L	≥0.2	>0.2-0.02	>0.02-0.002	>0.002-0.0002	≤0.0002 in one genus	≤0.0002 in different genera
	terrestrial non-mammals - sub-chronic NOEL, mg/kg	≥1000	>100-1000	>10-100	>1-10	≥1	≥1
	chronic NOEL, mg/kg	≥500	>50-500	>5-50	>0.5-5	≥0.5 in one genus	≥0.5 in different genera

TABLE B-2 SCORING CRITERIA FOR PHASE 3 VECTOR ELEMENTS

ELEMENT NUMBER	Units	0	2	4	6	8	10
P3E10	sub-lethal effects on plants - aquatic species						
	EC ₅₀ , mg/L ≥ 100		>10-100	>1-10	>0.1-1	0.01-0.1	<0.01
	NOAEC, mg/L ≥ 10		>1-10	>0.1-1	>0.01-0.1	0.001-0.01	<0.001
	terrestrial species						
	EC ₅₀ , mg/L water ≥ 100		>10-100	>1-10	>0.1-1	0.01-0.1	<0.01
	mg/m ³ air ≥ 100000		>10000-100000	>1000-10000	>100-1000	10-100	<10
	mg/kg soil ≥ 1000		>100-1000	>10-100	>1-10	0.1-1	<0.1
	NOAEC						
	mg/L water ≥ 10		>1-10	>0.1-1	>0.01-0.1	0.001-0.01	<0.001
	mg/m ³ air ≥ 10000		>1000-10000	>100-1000	>10-100	1-10	<1
	mg/kg soil ≥ 100		>10-100	>1-10	>0.1-1	0.01-0.1	<0.01
	OR						
	narrative	no measurable effects	Reversible effects such as enzyme induction and sub-cellular effects	Reversible effects, not dysfunctional	Degenerative reversible effects, slightly dysfunctional	Reversible dysfunctional pathological effects	Irreversible dysfunctional pathological effects

TABLE B-2 SCORING CRITERIA FOR PHASE 3 VECTOR ELEMENTS

ELEMENT NUMBER	Units	0	2	4	6	8	10
P3E11	sub-lethal effects on mammals - oral NOEL mg/kg ihl NOEL mg/m	>1000 >3000	>100-1000 >300-3000	>10-100 >30-300	>1-10 >3-30	>0.1-1 >0.3-3	<0.1 <0.3
P3E12	narrative mg/kg	No terata at >1000	Terata or developmental anomalies at >50-1000	Terata or developmental anomalies at >10-50	Terata or developmental anomalies at >1-10	Terata at >0.1-10	Terata at ≤0.1
P3E13	narrative	No evidence of genotox. or mutagen. with adequate testing	Positive results in <u>in vitro</u> only	Genotox./mutagen. in prokaryotic systems only	Effects on DNA, but no direct DNA interactions	Clastogenic effects but no direct interactions with DNA	Genotoxic/mutagenic usually with direct interactions with DNA

TABLE B-2

SCORING CRITERIA FOR PHASE 3 VECTOR ELEMENTS

ELEMENT NUMBER	Units	0	2	4	6	8	10
P3E14	narrative	No tumours in adequate studies, and does not interact with genetic material	Tumours in one species, and negative in others, and does not interact with genetic material	Tumours in more than one species, and does not interact with genetic material	Tumours in bioassays at doses causing metabolic saturation, or associated with lesions that pre-dispose to tumours. No interaction with DNA	Indirect acting carcinogen, no interaction with genetic material	Direct acting carcinogen that interacts with genetic material
a	P3E1	Concentrations in air					
	P3E2	Concentrations in water					
	P3E3	Concentrations in soils					
	P3E4	Concentrations in sediments					
	P3E5	Concentrations in plants					
	P3E6	Concentrations in animals					
	P3E7	Frequency of dispersion					
	P3E8	Acute lethality					
	P3E9	Sub-lethal effects on non-mammalian species					
	P3E10	Sub-lethal effects on plants					
	P3E11	Sub-lethal effects on mammals					
	P3E12	Teratogenicity					
	P3E13	Genotoxicity/Mutagenicity					
	P3E14	Carcinogenicity					
	P3E15	Undesirable aesthetic properties					

APPENDIX C - QSAR IN TOXICOLOGY - A REVIEW OF CURRENT LITERATURE

Appendix C

QSAR in Toxicology - A Review of Current Literature

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1.0 Introduction

With the ever-increasing production of new chemicals and the plethora of chemicals presently in use it has become impossible to experimentally assess the environmental and biological impact of most of them. The pressing need to evaluate the risks involved with the use of chemicals and their potential for environmental contamination has led to intense interest in quantitative structure-activity relationship (QSAR) studies. These studies attempt to mathematically define the relationship between a specific biological end point induced by a chemical and its physical and/or chemical properties. The idea that structure is related to biological activity originated with Crumb-Brown and Frazer in 1868. There are now several well-developed systems describing such relationships.

The determination of QSAR's requires a reliable measurement of a specific biological effect derived from dose-response data, as well as one or more molecular descriptors which quantitatively describe the physical properties and/or chemical structure of a compound. Various sets of physico-chemical and structural descriptors and combinations of the two have been used for QSAR studies. There have also been several statistical computer-based approaches used to analyze QSAR relationships. Physico-chemical and structural features of a wide range of compounds have been related to such biological endpoints as carcinogenicity, mutagenicity, toxicity, bioaccumulation, mixed-function oxidase induction and others. The accuracy and reliability of measurements, the significance of the biological endpoint, and the accuracy of descriptor measurement or calculation must be assessed when analyzing or using information resulting from QSAR studies. Once QSAR data can be used with confidence it will be a valuable tool when applied in conjunction with the screening system approach to identify those compounds which may present a significant hazard and require experimental assessment and regulation.

2.0 Types of QSAR Studies

There are three main types of studies which have been used with varying degrees of success to generate structure activity relationships: 1. the systematic/intuitive approach; 2. the extrathermodynamic approach; and 3. the connectivity approach.

2.1 The Systematic/Intuitive Approach

The systematic approaches to generating structure activity relationships are developed by studying a particular biological response to a homologous series of compounds. The compounds in the series should differ from each other in a systematic way so that the change in biological response can be attributed directly to a particular structural change. Structural differences between compounds in a series may include chain length (Bengtsson

et al., 1984), nature of the functional group at a specific position on the molecule (Vance et al., 1985), or nature of the functional groups at several selected positions on the molecule (Balaz et al., 1985 and Sturdik et al., 1985). The more complicated differences between compounds become, the more difficult it is to determine the relationship between the structural feature and the biological response. Thus this approach is limited to rather small groups of very closely related chemicals. Although not having widespread predictive capabilities, the results of systematic QSAR studies may provide valuable insights into the mechanisms of action of chemicals studied using this approach. (Vance and Levin, et al., 1984, Balaz et al., 1985, Sturdik et al., 1985, and Vance et al., 1985).

2.2 The Extrathermodynamic Approach

The extrathermodynamic approach was pioneered by Hansch and Fujita (1964) and involves the correlation of physico-chemical parameters with biological response. The parameters (known as descriptors) which may be used are: 1. hydrophobicity (including log P); 2. electronic parameters; 3. steric properties (e.g., topological characteristics, molecular shape and volume, molar refractivity, molecular weight and density); and 4. quantum variables (Frierson et al., 1986). These descriptors are combined in a mathematical expression derived from a multiple regression analysis which relates the measured biological response to the combination of parameters (Craig and Enslein et al., 1981). Once such a mathematical relationship has been generated it may be used to predict the biological response of an untested chemical.

The extrathermodynamic approach has some limitations. It can only be used successfully with congeneric databases since detailed structural features of the molecules are not used as descriptors (Frierson et al., 1986). Many of the physico-chemical parameters are dependent on each other resulting in undesirable colinearity among variables. This causes statistical bias and therefore orthogonal variables are preferred (Frierson et al., 1986 and Burkhard et al., 1983). This approach may not be appropriate for new chemicals since much of the required information may be unavailable.

2.3 Connectivity Methods

Connectivity methods produce descriptors based on the physical structure or substructure of a chemical. Several different methods have been developed for substructure representation and subsequent statistical analysis (Craig and Waite, 1976; Richman et al., 1978; Jurs et al., 1978; Lefkowitz et al., 1979; and Rosenkranz and Mermelstein, 1983). The descriptors used for this type of approach are derived solely from the chemical structure of the compound (Craig and Enslein, 1981; Burkhard et al., 1983; and Frierson et al., 1986). The most commonly used descriptors of this type are the molecular connectivity indices (Koch, 1983).

These describe the "connectedness" of the non-hydrogen atoms in a molecule based on the number of skeletal atoms, the degree of structural branching and the number of valence electrons of each skeletal atom (Koch, 1983). The molecular connectivity index was first defined by Kier and Hall (1976). Other types of substructure analysis have also been developed to represent the patterns of molecules, which make up chemical compounds (Craig and Waite, 1976 and Rosenkranz and Mermelstein, 1983). These methods are generally computer-assisted and therefore have the capacity to handle very large databases. Many studies have been done which combine the extrathermodynamic and the connectivity approaches; these will be discussed in section 3.

3.0 Biological Endpoints Examined

3.1 Carcinogenicity

There are three major computer-based QSAR systems which have been used to relate chemical structure to carcinogenic potential: a) the Enslein method (Enslein and Craig, 1978); b) automated data analysis using pattern recognition techniques (ADAPT) (Stuper et al., 1977); and c) computer automated structure evaluation (CASE) (Rosenkranz and Mermelstein, 1983)

3.1.1 The Enslein Method

The Enslein approach uses an extensive dictionary of molecular fragments. The computer chooses those fragments which are present in the chemical to be analyzed together with selected physico-chemical parameters. A large number of compounds for which the biological response is known are used as the "training set", which the computer program analyzes in order to determine which particular structural and physico-chemical features are related to the biological response (e.g., carcinogenicity). Structural and physico-chemical information describing a chemical of unknown carcinogenic potential may be entered and will be compared with the training set data and a prediction of biological activity will be made (Craig and Enslein, 1981). This method has been tested on 343 compounds from the IARC database, 223 of which are known carcinogens and 120 of which are known non-carcinogens (Enslein and Craig, 1982). The system correctly classified 87-91% of the carcinogens and 78-80% of the non-carcinogens. Some compounds were seriously misclassified if they did not possess features present in the training set (Frierson et al., 1986).

3.1.2 The ADAPT Method

The ADAPT program has been used to analyze several carcinogen databases. Various combinations of descriptors including fragment, substructure, molecular connectivity, environment (based on nearest neighboring atoms), atomic changes, hydrophobicity and molar refractivity have been employed (for reviews, see

Stuper et al., 1977 and 1979 and Jurs et al., 1978). The ADAPT program uses pattern recognition techniques to search for a discriminant which separates carcinogens from non-carcinogens (Chou and Jurs, 1979). This program correctly separated 90-95% of carcinogens from non-carcinogens within a group of 209 chemicals. Using a random set of 30 chemicals, its predictive value was 85.3%, with carcinogens being identified 90% of the time and non-carcinogens being identified 78% of the time (Jurs et al., 1979). In another study of 118 carcinogenic N-nitroso compounds and 35 non-carcinogens, the system was found to place 91% of the carcinogenic compounds correctly using 15 descriptors (Chou and Jurs, 1979). This study was repeated using 112 N-nitroso carcinogens and 38 non-carcinogens with the addition of a symmetry parameter. This increased correct placement of carcinogens to 93%. The overall predictive ability was 86% (Rose and Jurs, 1982). Analysis of a database made up of 200 PAHs using 28 descriptors which encompassed a substructure representation of the bay region, log P, volume and shape parameters, number of rings and electronic description of the bay region yielded a 96% correct separation of carcinogens from non-carcinogens. In a predictive trial 90% of the compounds were classified correctly (Yuan and Jurs, 1980). The overall predictive ability for carcinogenic potential in an aromatic amine database comprised of 157 compounds was found to be 85-90% (Yuta and Jurs, 1981).

3.1.3 The CASE Method

The CASE Program uses only substructure descriptors. These are generated by breaking each molecule in the database into every possible fragment containing 3-10 continuously joined atoms along with their attached hydrogen atoms (Frierson et al., 1986). The fragments are labeled to indicate bond types, functional groups, and whether they came from an active or inactive molecule. The CASE Program removes redundant fragments and separates those which remain into pools containing active or inactive fragments. Fragments occurring with equal probability in both pools are removed. Fragments are compared in pairs to determine whether any fragment is more or less potent in conjunction with another fragment. The activity of a new compound is predicted based on the probability that fragments overlapping with those in the training set are relevant to activity. Two PAH databases have been analyzed using CASE and in both cases 86% of the compounds were correctly placed, (Klopman, 1984 and Klopman et al., 1985b). A database containing 200 PAHs that was analyzed using ADAPT (Yuan and Jurs, 1980) was also analyzed using CASE, to compare the two systems (Klopman and Frierson, 1986). With ADAPT, 95% of 200 PAHs were correctly placed as carcinogens using 28 descriptors, while 89% were correctly placed using CASE. Although CASE did not predict as well as ADAPT for this database, CASE was more versatile since only the structure of the compounds were required. ADAPT requires prior knowledge about the compound from the researcher and is therefore more accurate with well studied

databases (Frierson et al., 1986). CASE is also less restricted than the Enslein approach since CASE creates its own set of fragments and does not rely on an independent dictionary (Frierson et al., 1986).

3.2 Mutagenicity

Structure-activity relationships in mutagenesis have been studied by computer based connectivity methods and by the systematic/intuitive approach.

An early study by Kier and Hall (1976) using molecular connectivity indices demonstrated the potential usefulness of such an approach by explaining 75% of the variance among the structures of 99 mutagens. This was improved upon by Enslein and Craig (1979) who used descriptors for molecular weight, log P and substructure with a database of 250 chemicals. Using this system they were able to correctly place 90% of strong mutagens and 96% of weak or non-mutagens. When substructure analysis was used alone on a 416 compound database from the Environmental Mutagen Information Centre there were 10.9% false negatives and 7.9% false positives (Craig and Enslein, 1981). A larger study involving 523 chemicals, placed 86% correctly from a training set of 301 mutagens and 208 non-mutagens. In a predictive trial, 80% of 37 mutagens and 23 non-mutagens were correctly classified (Enslein et al., 1983).

The CASE Program was used by Klopman and Rosenkranz (1984) to correlate structure with mutagenicity as measured by the Ames Salmonella assay of fifty-three nitroarenes tested for mutagenic potential, 26 were mutagenic, 22 were non-mutagenic and 5 were marginally mutagenic. Eighty-nine percent were correctly classified. Most of these compounds which were incorrectly classified had more than five rings, and it may have been possible that they were mutagenic, but not easily able to cross the cell membrane. A similar study was undertaken with mono- and polycyclic aromatic amines (Klopman et al., 1985b). Eighty chemicals were tested in S. typhimurium strain TA98 and 107 were tested in strain TA100. Eighty-eight percent of the TA98 database was correctly placed by CASE as was 84% of the TA100 database. A predictive trial with 19 compounds from the TA98 database which were held back from the training set indicated that the system has a predictive value of 84%. The CASE fragment analysis led to two general conclusions regarding mutagen structure: 1. substitution of the nitro group with an alkyl group lead to deactivation and 2. the fragment $-CH_2CH_2OH$ had a deactivating effect whether the nitro function was intact or not. These types of observations may lead to a better understanding of mechanisms of mutagenic action, making this type of QSAR study valuable as a mechanistic as well as a predictive tool.

The systematic approach has been used to study a set of 10 bifunctional nitrofluorene analogues each of which had a

different 2, 7-substitution pattern involving nitro, hydrogen, amino, hydroxy, methoxy or chlorine groups as the substituents (Vance *et al.*, 1985). Each of the 10 analogues was tested for mutagenicity in the Ames assay using *S. typhimurium* strain TA98 (wild-type for nitroreductase activity) and strain TA98NR (deficient in a specific nitroreductase activity). The purpose was to assess the importance of reduction of the nitro group and the effects of electron donating and electron withdrawing groups on mutagenic potency. It was concluded from this study that mutagenic potency is affected by the efficiency of nitroreduction of the nitro group, the stability of the proximate mutagen and the stability of the electrophile. The latter two being directly related to resonance stabilization effects. In a similar study using 17 structural homologous nitroarenes, Vance and Levin (1984) found that four structural features affected mutagenicity. These were: 1. physical dimensions of the ring; 2. isomeric position of the nitro group; 3. conformation of the nitro group with respect to the plane of the ring; and 4. the ability to resonance stabilize the ultimate electrophile. Although the conclusions reached from these types of studies are intuitive they do have some predictive value and should permit a first approximation in assessment of mutagenic potency of nitroaromatics (Vance and Levin, 1984).

These SAR studies also provide valuable mechanistic information. A series of 2-substituted 5-nitro furans have also been studied using this systematic approach (Balaz *et al.*, 1985 and Sturdik *et al.*, 1985). A total of 42 analogues were examined and some general conclusions relating structure to mutagenic effects were made. Mutagenic potential decreased with increasing length of alkyl residues. N-alkyl substituted esters were more mutagenic than the corresponding amides, and substitution of the 5-nitro group led to loss of mutagenic potential. With this type of approach it is hoped that information regarding the genotoxic properties of groups of homologous compounds can be elucidated (Balaz *et al.*, 1985).

3.3 Toxicity

QSAR studies have been used with a variety of chemicals in the field of aquatic toxicology. Various structural and physicochemical parameters have been correlated with toxic effects on several aquatic organisms.

A congeneric series of 28 unsubstituted PAHs were assessed for toxic effects in *Daphnia* (Govers *et al.*, 1984). A negative correlation was found to exist between log LC50 and a lower order molecular connectivity index ($r = 0.9972$ to 0.9970) as well as between log LC50 and log P ($r = 0.0089$ to 0.9975). These high correlation coefficients are encouraging but they may be somewhat misleading since a small data set was used (Govers *et al.*, 1984). The correlation between the 48 hour LC50 for *Daphnia*, and aqueous solubility and chain length of 33 hydrocarbons and chlorinated

hydrocarbons was sought by Bobra et al (1983). A near linear relationship between solubility and LC50 was observed over several orders of magnitude for straight chain hydrocarbons, but the relationship was not as strong for PAHs. A secondary factor which correlated with toxicity was molecular shape (ring number or chain length). A heterogeneous set of N-substituted PAHs was assayed for growth inhibiting ability with Tetrahymena pyriforms to generate 60 hr IGC50 values (Schultz and Applehans, 1985). A very poor correlation between IGC50 and log P was observed indicating that log P is not a good predictor for a heterogeneous group. More molecular structure descriptors are required to split the chemicals into toxicologically meaningful groups. In the case of these N-substituted PAHs, separation into groups based on the presence or location of electron donating or withdrawing functional groups on the ring allowed good predictive ability using log P within groups.

The toxicity-structure relationships of organotin compounds have been examined by several groups of workers (Wong et al, 1982; Laughlin et al., 1984; Laughlin et al., 1985 and Vighi and Calamari, 1985). The three subclasses of organotin compounds, R_3SnX , R_2SnX_2 and $RSnX_3$ showed good correlation with log P when tested separately for toxic effects on Daphnia (Vighi and Calamari, 1985) and algae (Wong et al., 1982). A poor correlation with log P was found when all the organotin compounds were examined as one group (Vighi and Calamari, 1985 and Wong et al., 1982). When pKa was included as a descriptor, 98% of the variability among the mixed group was explained. This increased to 98% if the Taft steric parameter was also included (Vighi and Calamari, 1985). An approach using topology descriptors was found to be more useful than one using physico-chemical parameters for correlation to crab larvae LC50 values for 8 organotin compounds. (Laughlin et al., 1985). The molecular topology was derived using independent structural parameters and was used to compute the surface area of the molecules. The correlation coefficient for topological surface area and LC50 was $r = 0.922$ for this small data set.

Structure activity relationships of a series of substituted pyridines have been studied using 8 physico-chemical descriptors and molecular connectivity indices. Multiple regression analysis (Schultz and Moulton, 1985) and principle components analysis (Moulton and Schultz, 1986) were used to analyze the data. Using multiple regression analysis the best single predictor of toxicity was found to be molar refractivity. The best two variable equation derived included a molar refractivity term and a hydrogen-accepting-ability term. The main drawback to using multiple regression analysis including all the variables is that additivity is assumed. This may not be valid for all compounds, especially those with complex multisubstituents (Schultz and Moulton, 1985). It was expected that the use of principal component analysis would yield more valid results (Moulton and Schultz, 1986). Principal component analysis identified four

clusters of variables and four new orthogonal variables were derived. The most important predictive variables were found to be molar refractivity, molecular connectivity, hydrophobicity and ability to accept or donate hydrogen atoms.

The relationship between 48 hour fish LC50 and log P, molecular weight, organic and inorganic characters and molecular connectivity indices was studied for a heterogeneous set of 123 organic chemicals. The best correlation was found between molecular connectivity indices and log LC50 ($r = 0.829$). A combination of molecular connectivity indices and log P yielded an improved correlation with log LC50 ($r = 0.876$). From this data it appears that the simplest way to predict the behaviour of a new chemical in a fairly reliable way is to measure log P and derive molecular connectivity indices (Yoshioka *et al.*, 1986).

The correlation between LC50 for various organisms and first and second order molecular connectivity indices was found to be fairly good for a mixed group of organic chemicals, and extremely good for a homologous group of chemicals (Koch, 1982).

A very strong correlation has been observed between log P and fish log LC50 for a series of chlorobenzenes and for a series of substituted phenols, all of which are chemicals for which narcosis is the mode of toxic action (McCartny *et al.*, 1985). The effect on toxicity due to substitution has been studied using 69 substituted benzenes (Hall *et al.*, 1984). It was concluded from this study that the contribution from individual substituents was constant and of magnitudes which decrease in the following order: $\text{Cl} > \text{Br} > \text{NO}_2 > \text{CH}_3 > \text{OCH}_3 > \text{NH}_2 > \text{OH}$. The overall contribution to toxicity by the substituents was found to be additive and an equation with a correlation coefficient of 0.951 was derived to express this additivity model with respect to LC50. The presence of the various substituents was found to be much more important than their actual position on the ring.

The main problem associated with the use of the techniques described in this report is that their predictive value is limited to groups of chemicals which fall between strict boundaries (Vighi and Calamari, 1985 and Laughlin *et al.*, 1984). These boundaries must be predetermined so that the appropriate descriptors can be used. This requires prior knowledge about a chemical so that it may be compared with chemicals of its own class (Schultz and Applehans, 1985). This type of information may not be available for new and untested chemicals.

3.4 Bioaccumulation

The extent of bioaccumulation by organisms depends on the uptake rate, the clearance rate and the time required to reach equilibrium (Hawker and Connell, 1985). Using a group of 21 organic chemicals, Hawker and Connell (1985) determined from experimental and theoretical values that clearance rate and uptake rate are in

a fixed relationship with the octanol/water partition coefficient in the range of 102.5 to 106. The relationship between log P and time to reach equilibrium was found to be linear for times less than one year (values in the literature have been extrapolated if log P is greater than 6). Bioaccumulation potential can be determined from uptake, clearance rates and time to reach equilibrium and these three parameters are directly related to log P in most cases. Therefore, it should be possible to predict bioconcentration factors directly from log P (Hawker and Connell, 1985). Positive relationships between log P and bioconcentration factors have been found for algae (Geyer *et al.*, 1984), roots (Briggs *et al.*, 1982), bacteria (Baughman and Paris, 1981), earthworms (Lord *et al.*, 1980), mussels (Geyer *et al.*, 1982), fish (Kenaga, 1980; Veith *et al.*, 1979; Kanazawa, 1981 and van Gestel *et al.*, 1985), and cattle (Geyer *et al.*, 1982). Log P has been used in conjunction with other parameters in order to predict bioconcentration factors. Govers *et al.*, (1984) measured bioconcentration factors for 28 unsubstituted PAHs in *Daphnia* and found a good correlation between log P and molecular connectivity indices and bioconcentration factors ($r = 0.9444$ to 0.9996). The actual prediction of bioconcentration factors was relatively unreliable, but possible ($r = 0.8318$ to 0.9628). For example published log P values range from 4.13 to 7.42 for hexachlorobenzene, from 3.98 to 6.19 for DDT, from 3.31 to 5.08 for methoxychlor and from 3.01 to 4.70 for naphthalene (Garten and Trabalka, 1983).

3.5 MFO Activity Induction

The ability of xenobiotics to induce mixed function oxidase (MFO) activity correlates well with their toxicity, thus measurement of MFO induction may allow prediction of toxicity (Safe, 1983). Structure-activity studies have been carried out which relate structure to MFO induction for inducers such as polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs) and polychlorinated dibenzo-p-dioxins (PCDDS). Bandiera *et al.*, (1982) examined the effect of changing the nature of the halogen substituent at the 4'-position of 2, 3, 4, 4', 5-pentachlorobiphenyl on arylhydrocarbon hydroxylase (AHH) induction. The induction potency was found to be dependent on the nature of the halogen substituent at the 4'-position with potency decreasing in the order $I > Br > Cl > F$. The different potencies may be explained by differences in polarizability of the laterally substituted halogen as well as differences in physico-chemical properties of the halogens. Halogen substitution was also shown to have an effect on the induction potency of analogues of 1, 4-bis [2-(3, 5-dichloropyridyloxy)]benzene, a phenobarbital-type inducer (Kelley *et al.*, 1985). Induction potency of the analogues decreased in the order $3, 5\text{-diBr} > 3, 5\text{-diCl} > 5\text{-Br} = 5\text{-Cl} > 3\text{-Cl} > \text{pyridyloxy}$. The most toxic PCB isomers are 3, 3', 4, 4'-tetra-, 3, 3', 4, 4', 5-penta- and 3, 3', 4, 4', 5, 5'-hexachlorobiphenyl. They are all AHH inducers and possess structural features which make them approximate isomers of the highly

toxic compound 2,3,7,8-tetrachlorodibenzo-p-dioxin. The more potent PCB AHH inducers appear to require chlorine substituents at both para positions; at least one meta position of both rings; and have no other substituents (Safe, 1983). The most potent methylcholanthrene (MC) - type inducers have 2 para-chloro, at least 2 meta-chloro, and 2 ortho-chloro substituents (Denomme *et al.*, 1983). All mono-ortho-chloro substituted derivatives of the 3 most highly active PCBs demonstrated mixed-type induction (Safe, 1983). Structure-activity studies with PBBs have indicated that AHH inducers must possess 3 lateral bromines with both para positions occupied and may also have one to four meta-chloro substituents as well as one ortho-chloro substituent (Robertson *et al.*, 1982). Structural features other than chlorine substitution have also been found to be important in relation to MFO induction. For instance, the optimal shape is flat (planar) and the optimal size is 3Å wide and 10Å long (Safe *et al.*, 1983). Hydrophobicity, molecular volume and polarizability may also affect activity (*ibid*).

All 209 PCB congeners were analyzed by a pattern recognition technique and principal component analysis applied (Clarke, 1986). Ten principal components were found to account for all the variability in the data set and three of these correlated well with MFO induction. A 3-dimensional plot of each of these three principal components was made for each PCB congener. Five distinct clusters of PCBs emerged from this plot. They were: 1. weak or inactive PB-type inducers; 2. primarily MC-type inducers; 3. primarily mixed-type inducers; 4. primarily PB-type inducers and; 5. entirely PB-type inducers. There were 12 outliers of which 3 were PB-type inducers and the rest were weak PB-type inducers or inactive. The clear groupings of most of the PCBs indicates a strong relationship between inducer type and structure. Two of the principle components tended to separate inducers from non-inducers and the third differentiated between inducer types. From this study, the author predicts that any PCBs found in groups 2 to 5 and outliers which have not been classified as inducers should be re-tested because of their structural similarities to active compounds (Clarke, 1986).

These studies of substitution patterns have shown that there is a relationship between structure and both induction-type and induction potency but they do not allow derivation of a quantitative relationship. The QSAR approach has been used to relate a hydrophobic, an electronic and a hydrogen-bonding parameter to the EC50 for 2, 3, 7, 8-TCDD receptor binding for 4'-substituted 2, 3, 4, 5-tetrachlorobiphenyls (Safe, 1983). An equation was derived using these parameters which had a correlation coefficient of $r = 0.916$. This study indicated that lipophilicity, H-bonding and electro-negativity play roles in receptor binding affinity. The EC50 for AHH induction in rat hepatoma cells in culture has been measured for 17 PCBs and correlated with hydrophobic, electronic, H-bonding and steric parameters (Bandiera *et al.*, 1983). The best correlation was found when all but the

steric descriptor were used in the derived mathematical expression. The existence of such a correlation indicates that it may be possible to predict whether a xenobiotic will induce MFO activity based on its physico-chemical nature.

3.6 Other Biological Endpoints

Ravanel et al., (1985) have studied the effect of structure of 23 chlorinated monophenols and their toxic effects on plant mitochondria. The structural descriptors used were molar refractivity, various steric and electronic parameters, melting point, molecular connectivity indices and log P. The toxic effects measured were inhibition of oxygen uptake, inhibition of electron transport and uncoupling of mitochondria. Increased uncoupling was observed as the number of chlorine atoms was increased or when nitro functions were added to 2-chlorophenols. No simple QSAR equation could be derived. It was noted that melting point had no effect on toxicity; electronic character played some role; and steric parameters were the most important. Log P alone or in combination with any other parameter did not satisfactorily explain a significant amount of the variability in the data. The unsatisfactory QSAR was probably due to the complex nature of the biological effect being measured (Ravanel et al., 1985).

A set of 14 glycol ethers were studied for their developmental toxicity potential using the in vitro hydra assay (Marshall et al., 1984). The developmental toxicity hazard index was greater than 1 (range 1.5 to 5.0) for 10 of the chemicals but no structure activity relationship was apparent.

In an extension of the scope of QSAR studies, Craig and Enslein (1981 b) have assessed the possibility of species to species extrapolation of toxicity data based on structural data. The interspecies differences were modeled by deriving an equation relating rat LD50 to mouse LD50, substructure descriptors, molecular weight and log P. 160 chemicals were used and the correlation coefficient for the prediction of rat LD50 from mouse LD50 was $r = 0.793$. These statistics could be improved by using a larger database of 600-800 compounds. The most important use for this type of species to species extrapolation would be extrapolation from test species to man. Some LD10 values for man are available from RTECS from poisoning cases therefore it may be possible to do rat or dog to man extrapolation studies (Craig and Enslein, 1981 b). An assessment of extrapolations of toxicity from animals to man has been done with anticancer agents and indicated that errors of 10% to ten-fold may be incurred (Willes et al., 1985).

4.0 Reliability of Descriptors and Biological Endpoints

Some of the problems which may be encountered with many QSAR studies have been discussed, such as colinearity of variables,

requirements for congeneric databases and the need for detailed physico-chemical data or other prior information about compounds before they can be analyzed. These limitations exist to greater or lesser degrees depending on the QSAR method used and on the nature of the chemical being studied and the database with which it is being compared. There are also other factors which are independent of the QSAR method being used which must be taken into account when results are interpreted. These are related to the reliabilities of the descriptors and the biological responses. It is important that the extent of accuracy of descriptor measurement and if possible the nature of the relationship between the descriptor and the biological response be known. It is also important to assess the accuracy of the measurement of the biological response as well as the actual reliability of the response.

4.1 Descriptors

One of the most commonly used descriptors is log P, particularly for bioaccumulation and aquatic toxicity studies. Log P must be used with caution because accurate predictions result only when toxicity is due to a general narcotic effect caused by partitioning of the chemical into biological membranes. If a specific toxic effect due to metabolic activation occurs, then the compound will be more toxic than predicted from log P data (Schultz and Moulton, 1985). An example of such a compound is 4-vinylpyridine, an alkylating agent which is more toxic than predicted from log P data accumulated for a series of substituted pyridines. Such an underestimation is due to the fact that the toxic effect of this compound is due not only to partitioning but to its ability to alkylate essential sulfhydryl groups on biological molecules (*ibid*).

A second potential problem with log P is accurate measurement. Widely different log P values for the same compound have been produced. For example, published log P values range from 4.13 to 7.42 for hexachlorobenzene; from 3.98 to 6.19 for DDT; from 3.31 to 5.08 for methoxychlor; and from 3.01 to 4.70 for naphthalene (Garten and Trabalka, 1983). It is therefore important to ensure that log P values included in any database to be used for predictive purpose be generated under rigidly standardized conditions.

Inaccuracy of QSAR measurements may result from the use of physico-chemical parameters if the compound being studied is metabolically activated and the values of the descriptors are significantly different for the active species than from the parent compound (Craig and Enslein, 1981). This type of problem may be reduced by using descriptors derived from substructure analysis. However, if the molecular fragments are drawn from a dictionary then inaccuracy may occur if the test chemical contains fragments not found in the dictionary (Frierson *et al.*, 1986).

4.2 Biological Endpoints

The measurements of most physico-chemical parameters and calculation of connectivity indices are usually very accurate, but biological measurements are not so, due to the complexity of biological systems (Koch, 1982). Application of QSAR to mutagens and carcinogens is particularly difficult since their biological activities are not well defined. For instance, mutagenesis as measured by short term tests such as the Ames assay is dependent on penetration of the cell membrane, metabolic activation, interaction with DNA, modification of DNA and DNA repair (Frierson et al., 1986). Due to the complex nature of the mutagenic response and the inherent inadequacies of short-term test systems there are likely to be some false-positive and false-negative results. Obviously the presence of such information in the training set data would confuse the structure-activity relationship somewhat. Inaccurate measurement can also be a problem when measuring toxicity endpoints. For example, compounds with a high log P value are accumulated more slowly by organisms than are those with low log P values. Toxicity is a function of the concentration of the active toxicant in the organism. Therefore, a short bioassay (eg. 96 hr. EC50) of chemicals with high log P values does not allow adequate correlation of the toxicity end point with physical/chemical properties since maximum concentrations of the chemical in the target tissues would not be reached within the time frame of the bioassay. Chemicals with high log P values would require long time periods (eg., several days to weeks) before steady-state concentrations would be reached in the target tissues (McCarty et al., 1985). This phenomenon should be considered when LC50 values are used as the biological endpoint for QSAR studies.

Measurements of bioconcentration factor is also subject to error and can usually be estimated only to within an order of magnitude. Since laboratory test situations are incapable of duplicating field conditions, bioconcentration factors used for predictive purposes must be generated under the same conditions as those which are contained in the database being used (Lyman et al., 1982).

Although it may be possible to generate satisfactory QSARs for various biological endpoints, it is important to consider the actual significance and reliability of the endpoint itself. Mutagenicity for example, is an endpoint which may have questionable significance and reliability. Mutagenicity is used as an indicator of genotoxic potential and those chemicals which exhibit genotoxicity are presumed to have greater carcinogenic. The significance of mutagenicity in relation to carcinogenicity has not yet been determined however, since neither the mechanism of carcinogenesis nor mutagenesis have been completely elucidated. If it is assumed that all mutagens are indeed carcinogens then the reliability of short-term mutagenicity tests

comes into question. A comparison of the Ames test with a DNA-repair test using 135 known carcinogenic and non-carcinogenic mutagens showed that the tests overlapped for 96 compounds and disagreed for 39 compounds. The reversion test was accurate for 64% of the chemicals and the repair test was accurate for 72% (De Floro et al., 1984). A review of studies which assessed the predictive capabilities of the Ames test found that from 62-99% of known carcinogens were found to be positive mutagens in the various studies reviewed (Rinkus and Legator, 1979). Problems are also encountered with carcinogenicity data, since most data have been produced from animal studies using different species, different dosing regimes and different definitions of the carcinogenicity endpoint. The current carcinogen databases are therefore not perfectly suited for QSAR studies because of variable methods and definitions used in data acquisition.

5.0 The Development and Use of QSAR

The development of QSARs must be undertaken in several stages. First the chemicals which will serve to fill the database must be chosen. Their biological effects must be properly quantified and must have been measured by consistent and accurate scientific methods. The molecular descriptors must be chosen according to predetermined guidelines and evaluated for reliability. The database containing the appropriate information regarding each chemical should be computerized and stored in a logical and accessible manner. The information in the database should then be analyzed in order to produce a mathematical equation to relate the biological effect to the molecular descriptors. Descriptor modifications may be required to improve the correlation between structure and activity. When a correlation has been established the system must be tested with a set of compounds of known biological activity which were not originally used to develop the correlation. If the predictive test is successful, then compounds of unknown biological activity may be tested. For more complete discussions of QSAR application, data management and analysis see Leo (1985), Loew et al., (1985), Stouch and Jurs (1985) and Weinstein et al., (1985).

6.0 Conclusion

Structure-activity relationships have been studied using a variety of approaches for several groups of chemicals. Biological endpoints which have been correlated with structure include carcinogenicity, mutagenicity, toxicity, bioaccumulation and MFO induction. Although very good correlations have been discovered in some cases, the predictive value of QSAR data has generally not been extremely good. This may be attributable to errors or variations in measurement of the biological endpoint, to inappropriate choice of descriptors or errors in descriptor measurement. Careful assessment of information used in the database as well as the use of larger databases and more sophisticated computerized analysis methods should improve the predictive capacity of QSAR

data. The QSAR approach appears to be very promising, but further development is required before predictions of the biological effects of new chemicals can be made with great accuracy and reliability.

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APPENDIX D

Contribution of Fugacity Models to Chemical Hazard Assessment

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This appendix contains introductory and explanatory material and full specifications concerning the contributions of fugacity models to the priority-setting process. Program listings are provided with sample input and output. Comments are included regarding possible future modifications and applications.

Introduction

The issue of the environmental behavior and effects of toxic chemicals is one of considerable interest to the public, to the chemical industry and to governments. A key concept which was first highlighted in Rachel Carson's "Silent Spring"¹ and which has emerged as an important regulatory consideration, is that many chemicals have the potential to migrate between the various media of air, water, soil, sediments and fish which comprise the environment. It is not always clear how a chemical will tend to partition, how long it will persist or which will be its dominant route to man. It is now generally accepted that it is possible to estimate these characteristics from readily available physical chemical properties using models.

This Appendix describes fugacity based computer models which use physical-chemical properties of chemicals to estimate multimedia partitioning of a contaminant, in this case in Ontario. In doing so the concepts of equilibrium partitioning, environmental reactions or degradation, advection and persistence are incorporated. The computed amounts and concentrations can be "scored" for use in scoring systems, or compared to concentrations which are judged to cause various toxicological effects thus introducing the concept of regulating emissions of toxic chemicals to quantities which are sufficiently low to ensure that adverse effects are avoided, or used to estimate human intakes.

The aims are to:

- (i) explain how the key chemical concepts of phase equilibrium, reaction and mass balancing under steady state conditions combine to control exposure and toxic effects; and

- (ii) suggest how these concepts may be used in hazard assessment procedures.

Tiered Testing

In common with other jurisdictions, Ontario has decided to adopt a tiered or multiphase approach in which chemicals are subjected to increasingly rigorous scrutiny, to extents dependent on their perceived hazard.

Phase 1 as described in this report provides an initial assessment of relevance to eliminate those chemicals which should obviously not be subjected to assessment because they are known to be absent, non-toxic or fall under other jurisdictions.

Phase 2 provides an assessment of toxicity and limited exposure estimation. At this stage a simple Level II version of the fugacity model is applied to determine the primary media in which the chemical is expected to partition and a first elementary depiction of the dominant environmental pathways. These characteristics result in a score being assigned characterizing environmental mobility. The model is described later as the "Phase 2" model.

In Phase 3 the chemical is subjected to more detailed exposure assessment to provide estimates of steady state environmental concentrations. In the event that actual monitored concentration data are available, they should supersede the calculated values or can be interpreted in conjunction with these data. This model is a version of the Level III fugacity model and includes intermedia transfer resistances and information about how the prevailing concentrations depend on the emissions into each medium.

Ultimately, it is expected that this model will be "fine tuned" or validated as a result of assessment experience.

The Subject Region

For assessment purposes it is necessary to define media volumes, areas and certain characteristics which influence partitioning tendencies. In this model the region is approximately that of the more industrialized and heavily populated Southern Ontario extending from Lakes Ontario and Erie on the south to the French-Ottawa Rivers in the north and from Lake Huron in the west to the Quebec border in the east. This should not be construed as neglecting Northern Ontario. The difficulty is that if the area of Northern Ontario is included it has the effect of "diluting" concentrations to low levels and giving a false sense of security. In fact, it is expected that the calculated concentrations will equally apply to regions such as Sudbury, Sault Ste. Marie or Thunder Bay. The aim is to select and justify media volumes which best characterize chemical fate. It is expected that as experience is gained the volumes and areas will be modified.

The total area considered is $200 \times 10^9 \text{ m}^2$ or 200,000 km². The air height is 2000 m giving an air volume of $400 \times 10^{12} \text{ m}^3$ or 400,000 km³. Of this area $120 \times 10^9 \text{ m}^2$ or 60% is land and $80 \times 10^9 \text{ m}^2$ or 40% is water including the inland lakes and parts of Lakes Ontario, Huron, Erie and St. Clair. The water volume is $4000 \times 10^9 \text{ m}^3$, corresponding to a mean depth of 50 m. This volume is heavily dominated by Lake Ontario. The accessible soil and terrestrial vegetation volume treated is $18 \times 10^9 \text{ m}^3$ corresponding to a depth of 0.15 m. The bottom sediment is $2.4 \times 10^9 \text{ m}^3$ corresponding to an active depth of 0.03 m.

The suspended sediment is calculated as 5 parts per million by volume of the water or $20 \times 10^6 \text{ m}^3$, while aquatic biota are similarly calculated as 1 part per million or $4 \times 10^6 \text{ m}^3$. Aquatic biota are treated as having the properties of fish but in reality represent primarily lower trophic levels.

The mean temperature is assumed to be 25°C since most data are obtained at that temperature. The organic carbon contents are: soil - 2%, bottom sediment - 4% and suspended sediment - 4% by mass. All solid media have a mean density of 1.5 g/cm^3 .

Fugacity

The models are based on the fugacity concept as more fully described in a series of papers by Mackay, Paterson and co-workers²⁻⁷. Fugacity is a thermodynamic quantity defined in units of pressure and is a measure of the partial pressure or escaping tendency of a chemical in a phase. Essentially, it is a potential quantity which characterizes the equilibrium partitioning of a mass in the same way that temperatures characterizes partitioning of heat. Heat flows from high to low temperature and similarly mass diffuses from high to low fugacity. When two phases are at equilibrium, their fugacities are equal and there is no net diffusion between phases.

Fugacity f (Pa) is related to concentration C (mol/m^3) by a fugacity capacity Z with units of $\text{mol/m}^3 \text{ Pa}$. The linear relationship is

$$C = fZ$$

Each chemical has a unique Z value for each phase which is dependent on the environmental temperature, the physical chemical properties of the substance and the nature of the phase into which it partitions.

A Z value is equivalent to "half" of a partition coefficient, i.e., the partition coefficient is the ratio of the two Z values. When equilibrium exists between Phases 1 and 2

$$K_{12} = C_1/C_2 = Z_1 f/Z_2 f = Z_1/Z_2$$

where K_{12} is the equilibrium partition coefficient.

Table 1 illustrates the relationship between physical chemical properties and Z values.

Table 1. Definition of Z values and illustrative values for Mirex

			Mirex values
Molecular weight	MW	g/mol	545.6
Vapor pressure	P*	Pa	1.33×10^{-4}
Aqueous solubility	C*	mol/m ³	1.28×10^{-7}
Octanol-water partition coeff.	K _{ow}		7.76×10^6
Bioconcentration factor	K _b		3.72×10^5
(correlation $K_b = 0.048 K_{ow}$) ⁹			
Organic carbon partition coeff.	K _{oc}		3.19×10^6
(correlation $K_{oc} = 0.411 K_{ow}$) ¹⁰			
Z ₁ Air	1/RT		4.03×10^{-4}
Z ₂ Water	C*/P*		9.64×10^{-4}
Z ₃ Soil	Z ₁ K _{oc} φ ₃ ρ ₃		92.3
φ = fraction organic content = 0.02			
ρ = density = 1.5 kg/L			
Z ₄ Bottom sediment	Z ₂ K _{oc} φ ₄ ρ ₄		184.7
φ = fraction organic content = 0.04			
ρ = density = 1.5 kg/L			
Z ₅ Suspended sediment	Z ₂ K _{oc} φ ₅ ρ ₅		184.7
φ = fraction organic content = 0.04			
ρ = density = 1.5 kg/L			
Z ₆ Biota (fish)	Z ₂ K _b ρ ₆		359
ρ = density = 1.0 kg/L			
T = 298 K			R = 8.314 J/mol K

Reaction rate, residence time or persistence is treated with two levels of detail. In phase 2 an overall persistence in days is assigned (or, if available, individual media persistences). In phase 3, each medium must be treated separately and reaction rate constants (day^{-1}) are entered where applicable. An overall persistence is calculated.

Phase 2 Model

The partitioning properties or Z values are thus estimated from the input data of

Molecular Mass	W g/mol
Water Solubility	S g/m^3 or mg/L
Vapor Pressure	P Pa
Octanol Water Partition Coefficient	K_{OW}

A simple environmental persistence is assigned, for example 30 days. This time may be attributable to reaction or advective flow or both. In the event that there is no reaction, a long half-life of 1×10^6 days can be entered which will give negligible reaction and avoid division by zero. (If individual media persistences are known they may be assigned and an overall weighted mean persistence will be calculated). The program incorporates advective residence times in air and water of 20 and 500 days respectively. The amount of chemical residing in the area at steady state (kg) is then the product of the emission rate (kg/day) and this persistence in days. The emission rate is estimated from the quantity used in Ontario (kg/day) and a

release factor corresponding to the fraction which is actually released to the environment. These quantities are scored elsewhere in Phase 2.

For example, a chemical used at a rate of 365,000 kg/year or 1000 kg/day released with a factor of 0.1 corresponds to an emission of 100 kg/day. If its persistence is 50 days a total of 5000 kg is expected to be distributed throughout Ontario between the various media.

The phase 2 distribution is estimated by assuming a common fugacity (f) to apply to the chemical in all media, thus if the total amount present is M moles (calculated from the mass above) then

$$M = \sum V_i Z_i f_i = f \sum V_i Z_i$$

$$\text{hence } f = M / \sum V_i Z_i$$

$$C_i = f Z_i \text{ mol/m}^3 \text{ (in each medium)}$$

$$M_i = C_i V_i \text{ mol (in each medium)}$$

The distribution of the chemical can thus be ascertained by amount or percent, the total $\sum M_i$ equalling M .

At this point it is apparent how the chemical will tend to partition, the media of primary concern can be identified and the probability of environmental mobility ascertained. For example, a chemical may be primarily discharged in water and show a tendency to volatilize to air. The scoring system described earlier ($P_2 E_4$) is essentially an expression of the capacity of

the chemical to be mobile and thus subject to appearance in media and regions other than that of local discharge. Table D-1 gives a comparison of chemical scores for this element using the fugacity level 2 model and the MOE scoring system.

Phase 3 Model

In Phase 3, the Z values are calculated as in Phase 2.

Persistence is treated in more detail. Reaction rate constants (day^{-1}) are expressed or requested for each medium and the corresponding half-lives calculated as $0.693/(\text{reaction rate constant})$.

The air and water advective residence times of 20 and 500 days are treated as corresponding to effective removal rate constants of 0.05 and 0.002 days^{-1} respectively. A bottom sediment burial rate of 1 mm/year is assumed corresponding to a rate constant of approximately 0.03 year^{-1} or 0.0001 day^{-1} . The reaction and advection rate constants are added for each medium to give a total removal rate constant. These values may be adjusted in the light of experience.

A weakness of this approach is that substantial quantities of certain chemicals may be advected into Ontario from other regions. If the inflow concentration is known it can be included in the calculation or the calculated concentration can be treated as being the value above this background. This subtlety is probably only a consideration for more detailed subsequent assessments which are beyond the scope of this study.

The major difference between the Phase 2 and 3 models is in their treatment of intermedia transfer. The Phase 3 model, which is essentially a

Level III fugacity model allows for different fugacities in each medium and for intermedia transfer resistances.

Diffusive transfer between phases i and j is given by

$$N = D_{ij}f_i - D_{ji}f_j$$

where N is the flux (mol/day) and D_{ij} (mol/m³ day) is a transfer coefficient. The D values can be calculated from mass transfer coefficients, interphase transfer areas, reaction rate constants and Z values. Methods of calculating D values are described by Mackay and Paterson⁵. Non-diffusive transfer such as sediment deposition or wet and dry deposition from the atmosphere can be also described by a D value calculated from a flow rate G (m³/day) and Z value⁶. These processes take place in one direction only.

The steady state mass balance for each compartment may be written

$$E_i + G_i C_{Bi} = V_i C_i K_i + \sum D_{ij} f_i - \sum D_{ji} f_j$$

where E_i is the emission rate (mol/day) and $G_i C_{Bi}$ is the inflow (mol/day) due to advection. The simultaneous linear equations for the desired number of compartments can be solved by a matrix inversion or in some cases by algebraic solution.

If it is necessary (for more detailed assessment) to consider time-varying emissions, a Level IV non-equilibrium model may be used. The set of differential equations for this model can be written

$$V_i dC_i/dt = E_i - V_i C_i K_i - \sum_j D_{ij} f_{ij} + \sum_j D_{ji} f_{ji}$$

These equations permit calculation of times to build to steady state, or to decay after emission reductions, to be determined. These calculations are useful in assessing potential long term contamination problems of new or existing substances.

The output of the Phase 3 model includes:

- concentrations in each medium
- intermedia transfer
- an overall persistence which is an appropriately weighted mean of the persistences of each medium.

Two typical "behaviour profiles" for benzene and acrylonitrile are given in Figures D-1 and D-2.

These data can be used to develop scores corresponding to concentrations in each medium, i.e., Scores P3E1 to P3E4. When actual environmental concentration data are available they can be used instead of or in conjunction with these estimated values. Table D-2 gives predicted and measured concentrations (where available) for the chemicals of concern. It is expected that discrepancies will exist between estimated and measured values which may have several causes.

- (1) Error in emission rates or release factors.
- (2) A tendency to measure concentrations in regions where the emission is of concern and thus of high concentration.
- (3) Errors in reaction or partitioning quantities.
- (4) Prevailing concentrations reflect past high emission rates (eg., mirex in Lake Ontario sediments).

At this stage it is not possible to assign probable extents of deviation between measured and predicted values, but as an indicator of likely success, it is observed that when a chemical is widely measured in space and time, it is observed that the mean concentration reflects a distribution which typically extends by a factor of 5 above and below the mean, thus an error of a factor of 20 is not unusual and 10 is quite frequent. No doubt, as more experience is gained these error limits can be reduced.

In addition to the scoring system the data can be used for two other purposes.

If a concentration which is "tolerable" or corresponds to a particular toxic end point is available (eg., 50 ppm of PCB in soil), then a safety ratio can be estimated as the ratio of this concentration to the estimated prevailing concentration. A large safety ratio corresponds to less hazard and reduced priority. In principle, such ratios can be assigned to all media and the medium of greatest concern can be identified.

Second, the dominant route of human uptake can be estimated by calculating for illustrative purposes the intake by inhalation, drinking water (which is assumed to be raw or untreated), and by ingestion of various foods. As has been discussed earlier in this report, there are doubts about the relationships between meat and vegetable concentrations and those of soils, water and atmosphere which influence them. But it is expected that reliable relationships will emerge in the next few years as the necessity for them becomes more apparent.

Copies of the two program listings with sample outputs are appended and diskettes compatible with an IBM-PC system are available from the authors.

Finally, it is emphasized that these models must be regarded as in a continuous state of development as new and more reliable expressions are established describing partitioning, reaction and intermedia transport. The models are primarily designed to treat organic chemicals which are not subject to dissolution or speciation changes. They can be used for dissociating organics and even for inorganic or metallic chemicals by careful selection of "equivalent" Z values but this must be done with extreme caution and the results subjected to thorough scrutiny for reasonableness.

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Figure D-1. Phase 3 Predicted Distribution of Benzene in S. Ontario

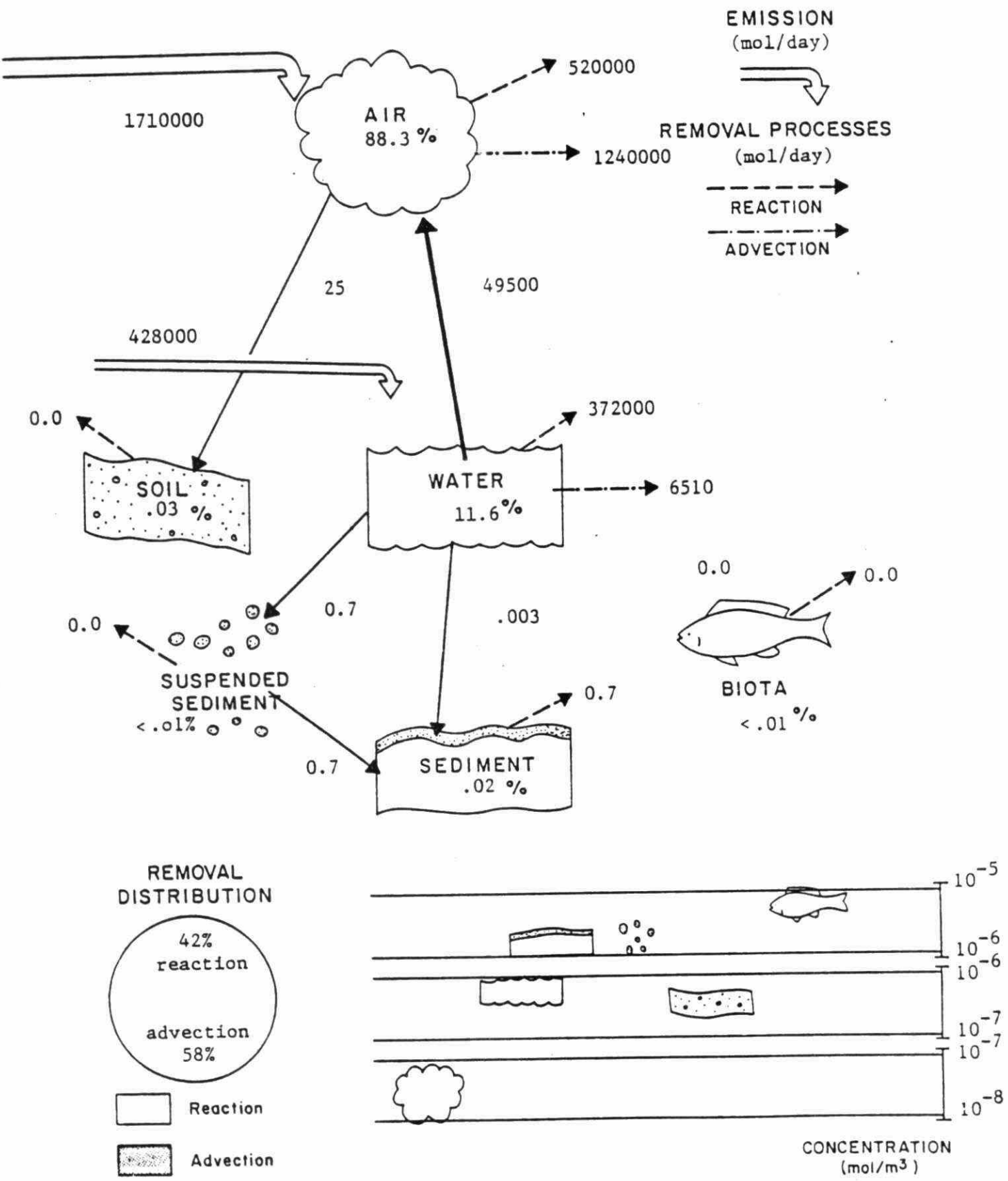
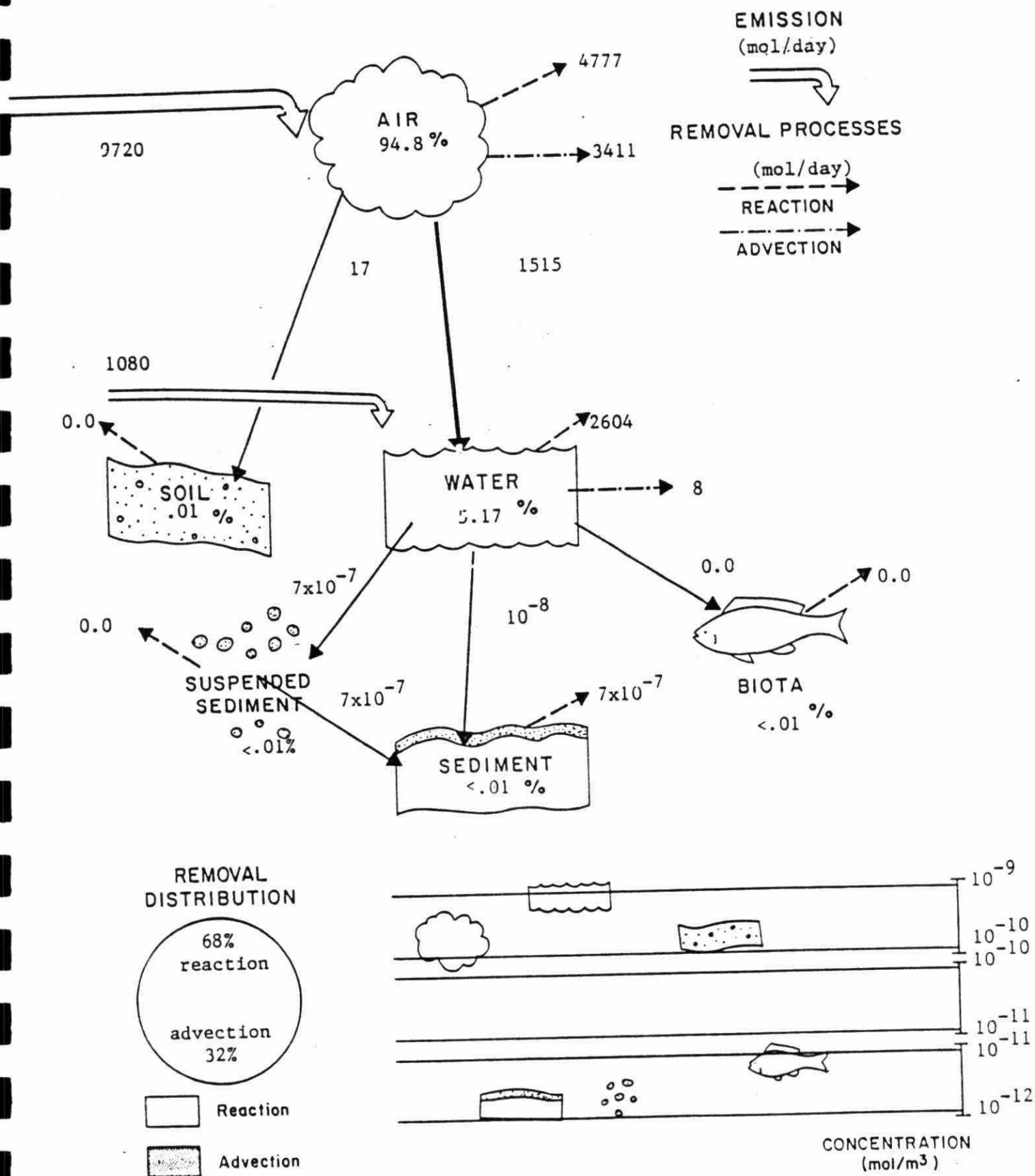


Figure D-2. Phase 3 Predicted Distribution of Acrylonitrile in S. Ontario



Phase 2 Output for Benzene using Individual Persistences

date: 11-15-1986

time: 15:12:11

Phase 2 calculation

benzene

compound properties

molecular weight 78.10 g/mol
 vapour pressure 1.2700E+04 pa or 1.2534E-01 atm or 9.5258E+01 mm Hg
 aqueous solubility 1.7600E+03 g/m3 or 2.2791E+01 mol/m3
 henry s constant 5.5723E+02 pa m3/mol
 octanol-water part coeff (log) 2.13 part coeff 1.349E+02
 temperature 25.0 deg C or 298.2 K

production rate

kg/year 6.1E+08
 mol/day 2.139863E+07

fraction entering environment

.1

emission rate

kg/year 6.1E+07 kg/day 167123.3
 mol/day 2139863

compartment	volume m3	z mol/m3.pa	density kg/m3
1 air	4.0000E+14	4.0342E-04	1.19
2 water	4.0000E+12	1.7946E-03	1000.00
3 soil	1.8000E+10	7.4622E-03	1500.00
4 sediment	2.4000E+09	7.4622E-03	1500.00
5 biota	4.0000E+06	1.1620E-02	1000.00

compartment	concn mol/m3	concn ug/m3	amount mol	amount kg	percent	reacted mol/day	adverted mol/day	persistent days
1 air	7.0385E-08	5.4971E+00	2.8154E+07	2.1988E+06	9.5655E+01	5.8654E+05	1.4077E+06	4.8000E+0
2 water	3.1311E-07	2.4454E+01	1.2524E+06	9.7814E+04	4.2552E+00	1.4313E+05	2.4798E+03	8.7500E-
3 soil	1.3020E-06	1.0168E+02	2.3435E+04	1.8303E+03	7.9622E-02	2.3435E-02	0.0000E+00	1.0000E-
4 sediment	1.3020E-06	1.0168E+02	3.1247E+03	2.4404E+02	1.0616E-02	3.1247E-03	0.0000E+00	1.0000E+0
5 biota	2.0274E-06	1.5834E+02	8.1095E+00	6.3335E-01	2.7552E-05	8.1095E-06	0.0000E+00	1.0000E-
Total			2.943E+07	2.299E+06	100.00	7.297E+05	1.410E+06	
fugacity		0.174E-03 Pa						

compartment	advective flow rate m3/day	advective residence time days
1 air	2.000E+13	2.000E+01
2 water	7.920E+09	5.051E+02

Phase 2 Output for Benzene using Overall Persistence

date: 11-15-1986

time: 15:14:43

Phase 2 calculation

benzene

compound properties

molecular weight 78.10 g/mol
 vapour pressure 1.2700E+04 pa or 1.2534E-01 atm or 9.5258E+01 mm Hg
 aqueous solubility 1.7800E+03 g/m3 or 2.2791E+01 mol/m3
 henry's constant 5.5723E+02 pa m3/mol
 octanol-water part coeff (log) 2.13 part coeff 1.349E+02
 temperature 25.0 deg C or 298.2 K

production rate kg/year 6.1E+08
 mol/day 2.139863E+07

fraction entering environment .1

emission rate kg/year 6.1E+07 kg/day 167123.3
 mol/day 2139863

compartment	volume m3	z mol/m3.pa	density kg/m3
1 air	4.0000E+14	4.0342E-04	1.19
2 water	4.0000E+12	1.7946E-03	1000.00
3 soil	1.8000E+10	7.4622E-03	1500.00
4 sediment	2.4000E+09	7.4622E-03	1500.00
5 biota	4.0000E+06	1.1620E-02	1000.00

compartment	concn mol/m3	concn ug/m3	amount mol	amount kg	percent	adverted mol/day
1 air	7.0363E-08	5.4954E+00	2.8145E+07	2.1981E+06	9.5655E+01	1.4073E+06
2 water	3.1301E-07	2.4446E+01	1.2520E+06	9.7784E+04	4.2552E+00	2.4790E+03
3 soil	1.3015E-08	1.0165E+02	2.3428E+04	1.8297E+03	7.9622E-02	0.0000E+00
4 sediment	1.3015E-06	1.0165E+02	3.1237E+03	2.4396E+02	1.0616E-02	0.0000E+00
5 biota	2.0267E-06	1.5829E+02	8.1069E+00	6.3315E-01	2.7552E-05	0.0000E+00

Total 2.942E+07 2.298E+06 100.00 1.410E+06

fugacity 0.174E-03 Pa

compartment	advective flow rate m3/day	advective residence time days
-------------	-------------------------------	----------------------------------

1 air	2.000E+13	2.000E+01
2 water	7.920E+09	5.051E+02

PHase 2 Output for Acrylonitrile using Individual Persistences

date: 11-14-1986

time: 14:35:29

Phase 2 calculation

acrylonitrile

compound properties

molecular weight 53.06 g/mol
 vapour pressure $1.3300E+04$ pa or $1.3126E-01$ atm or $9.9758E+01$ mm Hg
 aqueous solubility $3.7350E+05$ g/m³ or $7.0392E+03$ mol/m³
 henry's constant $1.8894E+00$ pa m³/mol
 octanol-water part coeff (log) -0.92 part coeff $1.202E-01$
 temperature 25.0 deg C or 298.2 K

production rate

kg/year $2.1E+07$
 mol/day 1084324

fraction entering environment

.01

emission rate

kg/year 210000 kg/day 575.3425
 mol/day 10843.24

compartment	volume m ³	z mol/m ³ .pa	density kg/m ³
1 air	$4.0000E+14$	$4.0342E-04$	1.19
2 water	$4.0000E+12$	$5.2926E-01$	1000.00
3 soil	$1.8000E+10$	$1.9614E-03$	1500.00
4 sediment	$2.4000E+09$	$1.9614E-03$	1500.00
5 biota	$4.0000E+06$	$3.0543E-03$	1000.00

compartment	concn mol/m ³	concn ug/m ³	amount mol	amount kg	percent	reacted mol/day	adverted mol/day	persistence days
1 air	$2.8480E-12$	$1.5111E-04$	$1.1392E+03$	$6.0445E+01$	$7.0823E+00$	$8.1370E+01$	$5.6959E+01$	$1.4000E+01$
2 water	$3.7364E-09$	$1.9825E-01$	$1.4945E+04$	$7.9301E+02$	$9.2916E+01$	$1.0675E+04$	$2.9592E+01$	$1.4000E+01$
3 soil	$1.3847E-11$	$7.3472E-04$	$2.4924E-01$	$1.3225E-02$	$1.5496E-03$	$2.4924E-07$	$0.0000E+00$	$1.0000E+01$
4 sediment	$1.3847E-11$	$7.3472E-04$	$3.3233E-02$	$1.7633E-03$	$2.0661E-04$	$3.3233E-08$	$0.0000E+00$	$1.0000E+01$
5 biota	$2.1562E-11$	$1.1441E-03$	$8.6248E-05$	$4.5763E-06$	$5.3621E-07$	$8.6248E-11$	$0.0000E+00$	$1.0000E+01$

Total

$1.608E+04$ $8.535E+02$ 100.00 $1.076E+04$ $8.655E+01$

fugacity

$0.706E-08$ Pa

compartment

advective flow rate
m³/day

advective residence time
days

1 air
2 water

$2.000E+13$
 $7.920E+09$

$2.000E+01$
 $5.051E+02$

Phase 2 Output for Acrylonitrile using Overall Persistence

date: 11-14-1986

time: 14:39:43

Phase 2 calculation

acrylonitrile

compound properties

molecular weight 53.06 g/mol
 vapour pressure 1.3300E+04 pa or 1.3126E-01 atm or 9.9758E+01 mm Hg
 aqueous solubility 3.7350E+05 g/m3 or 7.0392E+03 mol/m3
 henry's constant 1.8894E+00 pa m3/mol
 octanol-water part coeff (log) -0.92 part coeff 1.202E-01
 temperature 25.0 deg C or 298.2 K

production rate

kg/year 2.1E+07

mol/day 1084324

fraction entering environment

.01

emission rate

kg/year 210000 kg/day 575.3425

mol/day 10843.24

compartment	volume m3	z mol/m3.pa	density kg/m3
1 air	4.0000E+14	4.0342E-04	1.19
2 water	4.0000E+12	5.2926E-01	1000.00
3 soil	1.8000E+10	1.9614E-03	1500.00
4 sediment	2.4000E+09	1.9614E-03	1500.00
5 biota	4.0000E+06	3.0543E-03	1000.00

compartment	concn mol/m3	concn ug/m3	amount mol	amount kg	percent	advected mol/day
1 air	2.8568E-12	1.5158E-04	1.1427E+03	6.0632E+01	7.0823E+00	5.7135E+01
2 water	3.7479E-09	1.9886E-01	1.4992E+04	7.9546E+02	9.2916E+01	2.9683E+01
3 soil	1.3890E-11	7.3699E-04	2.5001E-01	1.3266E-02	1.5496E-03	0.0000E+00
4 sediment	1.3890E-11	7.3699E-04	3.3335E-02	1.7688E-03	2.0661E-04	0.0000E+00
5 biota	2.1629E-11	1.1476E-03	8.6515E-05	4.5905E-06	5.3621E-07	0.0000E+00
Total			1.613E+04	8.561E+02	100.00	8.682E+01

fugacity

0.708E-08 Pa

compartment

advective flow rate
m3/day

advective residence time
days

1 air	2.000E+13	2.000E+01
2 water	7.920E+09	5.051E+02

overall persistence 0.150E+01 days
 flow and reaction time 0.149E+01 days

Phase 3 Output for Benzene

date: 11-17-1986

time: 11:44:12

Phase 3 calculation

benzene

compound properties

molecular weight 78.10 g/mol
 aqueous solubility 1.7800E+03 g/m3 or 2.2791E+01 mol/m3
 vapour pressure 1.2700E+04 pa or 1.2534E-01 atm or 9.5258E+01 mm Hg
 henry's constant 5.5723E+02 pa m3/mol
 octanol-water part coeff (log) 2.13 part coeff 1.35E+02
 temperature 25.0 deg C or 298.2 K

compartment	volume m3	z mol/m3.pa	density kg/m3	amount mol	percent	mol/m3	concentrations microg/g	microg/m3
1 air	4.0000E+14	4.0342E-04	1.19	2.477E+07	88.34	6.191673E-08	4.074335E-03	4.835698
2 water	4.0000E+12	1.7946E-03	1000.00	3.255E+06	11.61	8.137336E-07	6.355259E-05	6.355259
3 soil	1.8000E+10	2.9849E-03	1500.00	8.240E+03	0.03	4.577706E-07	2.383459E-05	3.575189E+
4 sediment	2.4000E+09	5.9698E-03	1500.00	6.496E+03	0.02	2.706861E-06	1.409372E-04	2.114058
5 susp aquat mat	2.0000E+07	5.9698E-03	1500.00	5.410E+01	0.00	2.704765E-06	1.408281E-04	2.112421
6 biota	4.0000E+06	1.1620E-02	1000.00	2.108E+01	0.00	5.268945E-06	4.115045E-04	4.115045E+
Total				2.804E+07	100.00			
				or 2.190E+06 kg				

flow and reaction time 13.11 days reaction persistence 31.39 days

summary of compartment mass balances (mol/day)

	emissions	inflow	reaction	outflow	transport	fugacity (pa)
air	1.710000E+06	0.000000E+00	5.211160E+05	1.238335E+06	-4.945048E+04	1.534804E-04
water	4.280000E+05	0.000000E+00	3.720390E+05	6.509868E+03	4.945119E+04	4.534370E-04
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	3.562927E-03	1.533626E-04
sediment	0.000000E+00	0.000000E+00	7.146112E-01	0.000000E+00	-7.146250E-01	4.534270E-04
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	1.474619E-04	4.530759E-04
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	-4.768372E-07	4.534370E-04
Total	2.138000E+06	0.000000E+00	8.931556E+05	1.244844E+06		

total input (emissions and inflow) 2.138E+06 mol/day 1.670E+05 kg/day
 total output (reactions and outflow) 2.138E+06 mol/day 1.670E+05 kg/day

Phase 3 Output for Benzene (cont'd)

rate constant matrix (day⁻¹)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	2.100000E-02	0.000000E+00	0.000000E+00	0.000000E+00	4.100000E-05	2.104100E-02
water	0.000000E+00	4.300000E-03	0.000000E+00	1.100000E-01	0.000000E+00	1.143000E-01
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	1.100000E-04	1.100000E-04
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00

specific reaction rate (mol/m³day)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	1.300251E-09	0.000000E+00	0.000000E+00	0.000000E+00	2.538586E-12	1.302790E-09
water	0.000000E+00	3.499055E-09	0.000000E+00	8.951069E-08	0.000000E+00	9.300974E-08
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	2.977547E-10	2.977547E-10
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00

total reaction rate (mol/day)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	5.201005E+05	0.000000E+00	0.000000E+00	0.000000E+00	1.015434E+03	5.211160E+05
water	0.000000E+00	1.379622E+04	0.000000E+00	3.580428E+05	0.000000E+00	3.720390E+05
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	7.146112E-01	7.146112E-01
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00

transformation (percent)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	58.231790	0.000000	0.000000	0.000000	0.113691	58.345480
water	0.000000	1.567053	0.000000	40.087390	0.000000	41.654440
soil	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
sediment	0.000000	0.000000	0.000000	0.000000	0.000080	0.000080
susp aquat mat	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
biota	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000

mass balance (1 day)

	inflows	outflows	flow m ³ /day	inflow conc mol/m ³	residence time day
air	0.000000E+00	1.238335E+06	2.000000E+13	0.000000E+00	2.000000E+01
water	0.000000E+00	6.509868E+03	8.000000E+09	0.000000E+00	5.000000E+02
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity

Phase 3 Output for Benzene (cont'd)

transfer rate coefficients between compartments

No. compartment

1 air
2 water
3 soil
4 sediment
5 susp aquat mat
6 biota

compartment	D (mol/day*pa)	transport rate (mol/day)	interfacial area (m**2)	k(i,j) (m/day)	k(j,i) (m/day)	k overall	res(i,j)	res(j,i)	tau (day)
from 1 to 2	1.6494E+08	-4.9476E+04	8.0000E+10	1.2000E+02	1.2000E+00	2.0618E-03	0.000000	0.000000	28.5
from 2 to 1	1.6494E+08	4.9476E+04	8.0000E+10	1.2000E+00	1.2000E+02	2.0618E-03	0.000000	0.000000	28.5

from 1 to 3	2.1502E+08	2.5332E+01	1.2000E+11	2.4000E+02	4.5255E+00	1.7919E-03	0.000000	0.000000	0.
from 3 to 1	2.1502E+08	-2.5332E+01	1.2000E+11	4.5255E+00	2.4000E+02	1.7919E-03	0.000000	0.000000	0.

from 2 to 4	3.2182E+05	3.2349E-03	8.0000E+10	2.4000E-01	2.2627E-03	4.0228E-06	0.000000	0.000001	30.
from 4 to 2	3.2182E+05	-3.2349E-03	8.0000E+10	2.2627E-03	2.4000E-01	4.0228E-06	0.000001	0.000000	30.

compartment	D (mol/day*pa)	transport rate (mol/day)	tau(i,j)
from 2 to 5	1.9700E+06	7.1124E-01	0.04
from 5 to 2	1.9700E+06	-7.1124E-01	0.04

compartment	D (mol/day*pa)	transport rate (mol/day)	k2 (day-1)	tau(i,j) (day)
from 2 to 6	1.1052E+04	4.7684E-07	2.3777E-01	2.91
from 6 to 2	1.1052E+04	-4.7684E-07	2.3777E-01	2.91

compartments	by	D (mol/day*pa)	transport rate (mol/day)	flow (m3/day)	flow (m3/y)	tau(i,j) (day)	velocity (m/y)
from 3 to 2	water	1.6520E+05	2.5336E+01	9.2055E+07	3.3600E+10	2.254E+02	2.800E-01
from 3 to 2	soil	6.8693E-03	1.0535E-06	2.3014E+00	8.4000E+02	5.420E+09	7.000E-09
from 3 to 2	total	1.6520E+05	2.5336E+01			225.38	
from 5 to 4		1.5701E+03	7.1139E-01	2.6301E+05	9.6000E+07	52.70	

air molecular diffusivity	0.96E+00	m2/day	air effective diffusivity	0.34E+00	m2/day	porosity	0.5	mean path length	0.
water molecular diffusivity	0.96E-04	m2/day	water effective diffusivity	0.34E-04	m2/day	porosity	0.5	mean path length	0.

Phase 3 Output for Acrylonitrile

date: 11-17-1986

time: 11:56:50

Phase 3 calculation

acrylonitrile

compound properties

molecular weight 53.06 g/mol
aqueous solubility 3.7350E+05 g/m3 or 7.0392E+03 mol/m3
vapour pressure 1.3300E+04 pa or 1.3126E-01 atm or 9.9758E+01 mm Hg
henry's constant 1.8894E+00 pa m3/mol
octanol-water part coeff (log) -0.92 part coeff 1.20E-01
temperature 25.0 deg C or 298.2 K

compartment	volume m3	z mol/m3.pa	density kg/m3	amount mol	percent	mol/m3	concentrations microg/g	microg/m3
1 air	4.0000E+14	4.0342E-04	1.19	6.821E+04	94.82	1.705327E-10	7.633175E-06	9.048465E-
2 water	4.0000E+12	5.2926E-01	1000.00	3.720E+03	5.17	9.300689E-10	4.934946E-08	4.934946E-
3 soil	1.8000E+10	7.8458E-04	1500.00	4.867E+00	0.01	2.703895E-10	9.564579E-09	1.434687E-
4 sediment	2.4000E+09	1.5692E-03	1500.00	6.618E-03	0.00	2.757453E-12	9.754031E-11	1.463105E-
5 susp aquat mat	2.0000E+07	1.5692E-03	1500.00	5.511E-05	0.00	2.755258E-12	9.746264E-11	1.461940E-
6 biota	4.0000E+06	3.0543E-03	1000.00	2.147E-05	0.00	5.367307E-12	2.847893E-10	2.847893E-
Total				7.194E+04	100.00			
				or 3.817E+03 kg				

flow and reaction time 6.66 days reaction persistence 9.75 days

summary of compartment mass balances (mol/day)

	emissions	inflow	reaction	outflow	transport	fugacity (pa)
air	9.720000E+03	0.000000E+00	4.777713E+03	3.410654E+03	1.531634E+03	4.227197E-07
water	1.080000E+03	0.000000E+00	2.604193E+03	7.440552E+00	-1.531634E+03	1.757290E-09
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	-7.629395E-06	3.446316E-07
sediment	0.000000E+00	0.000000E+00	7.279677E-07	0.000000E+00	-7.395716E-07	1.757290E-09
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	-1.500666E-11	1.755890E-09
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	4.547474E-13	1.757290E-09
Total	1.080000E+04	0.000000E+00	7.381906E+03	3.418094E+03		

total input (emissions and inflow) 1.080E+04 mol/day 5.730E+02 kg/day
total output (reactions and outflow) 1.080E+04 mol/day 5.730E+02 kg/day

Phase 3 Output for Acrylonitrile (cont'd)

rate constant matrix (day-1)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	7.000000E-02	0.000000E+00	0.000000E+00	0.000000E+00	4.100000E-05	7.004100E-02
water	0.000000E+00	0.000000E+00	0.000000E+00	7.000000E-01	0.000000E+00	7.000000E-01
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	1.100000E-04	1.100000E-04
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00

specific reaction rate (mol/m3day)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	1.193729E-11	0.000000E+00	0.000000E+00	0.000000E+00	6.991841E-15	1.194428E-11
water	0.000000E+00	0.000000E+00	0.000000E+00	6.510482E-10	0.000000E+00	6.510482E-10
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	3.033199E-16	3.033199E-16
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00

total reaction rate (mol/day)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	4.774916E+03	0.000000E+00	0.000000E+00	0.000000E+00	2.796736E+00	4.777713E+03
water	0.000000E+00	0.000000E+00	0.000000E+00	2.604193E+03	0.000000E+00	2.604193E+03
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	7.279677E-07	7.279677E-07
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00

transformation (percent)

compartment	photolysis	oxidation	hydrolysis	biodegradation	other	total
air	64.684050	0.000000	0.000000	0.000000	0.037886	64.721940
water	0.000000	0.000000	0.000000	35.278060	0.000000	35.278060
soil	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
sediment	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
susp aquat mat	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
biota	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000

mass balance (1 day)

	inflows	outflows	flow m3/day	inflow conc mol/m3	residence time day
air	0.000000E+00	3.410654E+03	2.000000E+13	0.000000E+00	2.000000E+01
water	0.000000E+00	7.440552E+00	8.000000E+09	0.000000E+00	5.000000E+02
soil	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity
sediment	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity
susp aquat mat	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity
biota	0.000000E+00	0.000000E+00	0.000000E+00	0.000000E+00	infinity

Phase 3 Output for Acrylonitrile (cont'd)

transfer rate coefficients between compartments

No. compartment

- 1 air
- 2 water
- 3 soil
- 4 sediment
- 5 susp aquat mat
- 6 biota

compartment	D (mol/day*pa)	transport rate (mol/day)	interfacial area (m**2)	k(i,j) (m/day)	k(j,i) (m/day)	k overall	res(i,j)	res(j,i)	tau(i,j) (day)
from 1 to 2	3.5985E+09	1.5148E+03	8.0000E+10	1.2000E+02	1.2000E+00	4.4982E-02	0.000000	0.000000	28.
from 2 to 1	3.5985E+09	-1.5148E+03	8.0000E+10	1.2000E+00	1.2000E+02	4.4982E-02	0.000000	0.000000	28.

from 1 to 3	2.1502E+08	1.6791E+01	1.2000E+11	2.4000E+02	4.5255E+00	1.7919E-03	0.000000	0.000000	
from 3 to 1	2.1502E+08	-1.6791E+01	1.2000E+11	4.5255E+00	2.4000E+02	1.7919E-03	0.000000	0.000000	
from 2 to 4	9.4912E+07	1.4901E-08	8.0000E+10	2.4000E-01	2.2627E-03	1.1864E-03	0.000000	0.000004	0.
from 4 to 2	9.4912E+07	-1.4901E-08	8.0000E+10	2.2627E-03	2.4000E-01	1.1864E-03	0.000004	0.000000	0.

compartment	D (mol/day*pa)	transport rate (mol/day)	tau(i,j)
from 2 to 5	5.1782E+05	7.2469E-07	0.04
from 5 to 2	5.1782E+05	-7.2469E-07	0.04

compartment	D (mol/day*pa)	transport rate (mol/day)	k2 (day-1)	tau(i,j) (day)
from 2 to 6	2.9089E+03	-4.5475E-13	2.3809E-01	2.91
from 6 to 2	2.9089E+03	4.5475E-13	2.3809E-01	2.91

compartments	by	D (mol/day*pa)	transport rate (mol/day)	flow (m3/day)	flow (m3/y)	tau(i,j) (day)	velocity (m/y)
from 3 to 2	water	4.8721E+07	1.6791E+01	9.2055E+07	3.3600E+10	2.009E-01	2.800E-01
from 3 to 2	soil	1.8056E-03	6.2227E-10	2.3014E+00	8.4000E+02	5.420E+09	7.000E-09
from 3 to 2	total	4.8721E+07	1.6791E+01			0.20	
from 5 to 4		4.1271E+02	7.2467E-07	2.6301E+05	9.6000E+07	52.70	

air molecular diffusivity 0.96E+00 m2/day air effective diffusivity 0.34E+00 m2/day porosity 0.5 mean path length 0.
water molecular diffusivity 0.96E-04 m2/day water effective diffusivity 0.34E-04 m2/day porosity 0.5 mean path length 0.

```

5 Phase 2 fugacity model
10 DIM V(10),Z(10),D(10),C(10),CH(10),PPH(10),P(10),A(10),AKG(10),OG(10)
15 DIM COMP$(10),MAT$(7)
20 DIM R(10,5),RT(10),RV(10,5),RTV(10),RK(10,5),RKT(10),RP(10,5),RPT(10)
25 DIM G(10),CB(10),GCB(10),GCO(10),GZ(10),RES(10),ZKI(10)
30 DEFINT I-J
35 N=5 number of compartments or media
40 definition of compartments
45 1-air,2-water,3-soil,4-sediment
50 5-biota
55 KEY OFF
60 CLS
65 PRINT "PHASE 2 FUGACITY CALCULATION"
70 PRINT "An interactive model using microsoft BASIC language.":PRINT " "
75 PRINT "NOTES":PRINT " "
80 PRINT "When using this model, it is immaterial whether values are entered"
85 PRINT "in exponential or non-exponential form,i.e. 2e04 or 20000":PRINT " "
90 PRINT "The results will be printed out on a printer, not on the screen"
95 PRINT "The print width required is 150 characters":PRINT " "
100 PRINT "If you enter an erroneous value, you must start again":PRINT " "
105 PRINT "The parameters required are:"
110 PRINT "molecular weight (g/mol),vapor pressure (Pa), solubility (g/m3),log Kow
115 PRINT "persistence (days)"
120 PRINT "We define the five compartments by numbers as follows"
125 PRINT "1-air,2-water,3-soil,4-bottom sediment"
130 PRINT "5-biota":PRINT " "
135 INPUT "press enter to continue";AZ$
140 CLS
145 PRINT "Note that compartment numbers are:"
150 PRINT "1-air,2-water,3-soil,4-bottom sediment"
155 PRINT "5-biota":PRINT " "
160 FOR I=1 TO 5:READ COMP$(I):NEXT I
165 DATA "air","water","soil","sediment","biota"
170 FOR I=1 TO 6:READ MAT$(I):NEXT I
175 DATA rate constant matrix (day-1),specific reaction rate (mol/m3day),total reaction rate (mol/day)
180 DATA transformation (percent),mass balance (1 hour),infinity
185 enter physical properties
190 PRINT "please input the chemical's physical-chemical properties":PRINT " "
195 INPUT "What is the compound's name?";COMP$(7):PRINT " "
200 INPUT "molecular weight (g/mol), eg. 100 g/mol";MW
205 INPUT "vapour pressure in Pa, eg. 10. (note vap press (Pa)=vap press (atm)x101325 or vap press (Pa)=vap press (mm Hg)x13.3)";VPP
210 INPUT "aqueous solubility in g/m3 or equivalent mg/L, eg. 50";SG
215 INPUT "log octanol-water partition coeff Kow, eg. 3.5 (note that it is the log that is requested)";PKOWL
220 INPUT "press enter to continue";ZAS$
225 CLS
230 TC=25!
235 RG=8.314
240 calculate properties
245 TKE=273.15+TC
250 RTT=RG/TKE
255 VPA=VPP/101325!:VPM=VPA*760
260 SM=SG/MW
265 H=VPP/SM:HD=H/RTT
270 FKOW=10!^PKOWL

```

```

275 'define areas and volumes
280 AREA=2E+11:AFW=.4:AF5=1-AFW
285 AR(1,2)=AFW*AREA:AR(1,3)=AF5*AREA:AR(2,4)=AR(1,2)
290 FOR I=1 TO N:FOR J=1 TO N:AR(J,I)=AR(I,J):NEXT J:NEXT I
295 V(1)=AREA*2000:V(2)=AR(1,2)*50:V(3)=AR(1,3)*.15
300 V(4)=AR(2,4)*.03:V(5)=V(2)*.000001
305 'define densities
310 D(1)=.029*101325!/RTT
315 D(2)=1000:D(3)=1500:D(4)=1500:D(5)=1000
320 'define organic content
325 ORG(3)=.05:ORG(4)=.05
330 'define partition coefficients
335 PKOC=PKOW*.411
340 PK32=PKOC*ORG(3)
345 PK42=PKOC*ORG(4)
350 PK52=.048*PKOW
355 'define dimensionless partition coefficients
360 PD32=PK32*D(3)/1000
365 PD42=PK42*D(4)/1000
370 PD52=PK52*D(5)/1000
375 'define fugacity capacities (mol/m3.pa)
380 Z(1)=1!/RTT
385 Z(2)=1!/H
390 Z(3)=PD32*Z(2)
395 Z(4)=PD42*Z(2)
400 Z(5)=PD52*Z(2)
405 'define advective flows (m3/day),background concns (mol/m3), calculate advective residence times (days) for air and water
410 G(1)=2E+13:CB(1)=0:RES(1)=V(1)/G(1)
415 G(2)=7.92E+09:CB(2)=0:RES(2)=V(2)/G(2)
420 CLS
425 WIDTH "lpt1":150
430 LPRINT CHR$(15)
435 LPRINT "date: ";DATE$;"time: ";TIME$:LPRINT " "
440 LPRINT "Phase 2 calculation":LPRINT " "
445 LPRINT COMP$(7):LPRINT " ":LPRINT "compound properties":LPRINT " "
450 LPRINT "molecular weight":TAB(40):USING "#####.## g/mol":WM
455 LPRINT "vapour pressure":TAB(40):USING "###.###^#### pa":VPP;
460 LPRINT USING " or ##.###^#### atm":VPA;
465 LPRINT USING " or ##.###^#### mm Hg":VPM
470 LPRINT "aqueous solubility":TAB(42):USING "##.###^#### g/m3":S6;
475 LPRINT USING " or ##.###^#### mol/m3":SM
480 LPRINT "henry's constant":TAB(40):USING "##.###^#### pa m3/mol":H
485 LPRINT "octanol-water part coeff (log)":TAB(34):USING "#####.##":PKOWL:
490 LPRINT USING " part coeff ##.###^####":PKOW
495 LPRINT "temperature":TAB(40):USING "#####.0 deg C":TC:
500 LPRINT USING " or #####.0 K":TKE:LPRINT " ":LPRINT " "
505 LPRINT " ":LPRINT " "
510 INPUT "input production rate (kg/year)":EK
515 EM=EK*1000/MM/365 'mol/day
520 INPUT "input fraction entering the environment":FR
525 'calculate emissions into environment
530 EE=EK*FR 'kg/year
535 EED=EE/365 'kg/day
540 E=EE*1000/MM/365 'mol/day

```

```

545 AT=0!:ZVKT=0!:GCBT=0:GZT=0:GCDT=0:RTVT=0
550 LPRINT "production rate";TAB(43) "kg/year";EK
555 LPRINT TAB(43) "mol/day";EH:LPRINT " "
560 LPRINT "fraction entering environment";TAB(50) FR:LPRINT " "
565 LPRINT "emission rate";TAB(43) "kg/year";EE:TAB(60) "kg/day";EED
570 LPRINT TAB(43) "mol/day";E:LPRINT " ":LPRINT " "
575 INPUT "Do you wish to enter an overall persistence (1) or individual persistences (2)";ZZ
580 IF ZZ=2 THEN GOTO 595
585 INPUT "Enter overall persistence in days";TP
590 GOTO 710
595 PRINT "enter persistence for each compartment in units of days"
600 PRINT "persistences are entered in the following sequence:-compartment no.,persistence, separated by commas (eg. 1,1000)"
605 PRINT "in this case a persistence must be entered for each medium, if unknown, enter a large number, eg 1e06 to indicate neg-
le reaction in tha
t medium"
610 PRINT "No.;"      Compartment"
615 PRINT "1;"      Air"
620 PRINT "2;"      Water"
625 PRINT "3;"      Soil"
630 PRINT "4;"      Sediment"
635 PRINT "5;"      Biota";PRINT " "
640 "convert persistence ZKI to reaction rate constant RK
645 FOR L=1 TO N
650 J=4
655 INPUT L,ZKI(I):ZK=1/ZKI(I):RK(I,J)=ZK
660 NEXT L
665 CLS
670 "calculate total reaction rate constants (day-1)
675 FOR I=1 TO N
680 RKT(I)=0
685 NEXT I
690 FOR I=1 TO N
695 FOR J=1 TO 5
700 RKT(I)=RKT(I)+RK(I,J)
705 NEXT J:NEXT I
710 FOR I=1 TO N
715 ZV(I)=Z(I)*V(I)
720 ZVT=ZVT+ZV(I)
725 NEXT I
730 IF ZZ=2 THEN GOTO 740
735 ZVKT=ZVT/TP:GOTO 765
740 FOR I=1 TO N
745 ZVK(I)=Z(I)*V(I)*RKT(I)
750 ZVKT=ZVKT+ZVK(I)
755 NEXT I
760 "calculate advective inflow GCB
765 FOR I=1 TO N
770 GZ(I)=G(I)*Z(I)
775 GZT=GZT+GZ(I)
780 GCB(I)=G(I)*CB(I)
785 GCBT=GCBT+GCB(I)
790 NEXT I
795 "calculate fugacity F (Pa)
800 F=(E+GCBT)/(ZVKT+GZT)

```

805 'calculate concns C (mol/m3), amounts A,AK6 (mol/kg) and advective outflow GCO (mol/day)

810 FOR I=1 TO N

815 C(I)=Z(I)*F

820 A(I)=C(I)*V(I)

825 AT=AT+A(I)

830 AK6(I)=A(I)*WM/1000

835 ATK6=AT*WM/1000

840 GCO(I)=G(I)*C(I)

845 GCOI=GCOI+GCO(I)

850 'calculate reaction rates RV (mol/day)

855 RT(I)=0

860 FOR J=1 TO 5

865 R(I,J)=C(I)*RK(I,J)

870 RV(I,J)=R(I,J)*V(I)

875 RT(I)=RT(I)+R(I,J)

880 RTV(I)=RT(I)*V(I)

885 RP(I,J)=100*RV(I,J)/(F*ZVKT)

890 RPT(I)=100*RTV(I)/(F*ZVKT)

895 NEXT J

900 NEXT I

905 FOR I=1 TO N

910 RTVT=RTVT+RTV(I)

915 P(I)=100*A(I)/AT

920 PT=PT+P(I)

925 PPM(I)=C(I)*WM*1000/D(I)

930 CM(I)=C(I)*WM*1000000!

935 NEXT I

940 'calculate total inflows EGIN and outflows R6DT (mol/day)

945 EGIN=E+GCOI

950 R6DT=RTVT+GCOI

955 'calculate overall persistence (days) due to advection and reaction

960 TR=AT/EGIN

965 IF ZZ=1 THEN GOTO 980

970 'calculate persistence (days) due to reaction only

975 IP=AT/RTVT

980 LPRINT "compartment";TAB(23) "volume";TAB(39) "z";TAB(51) "density"

985 LPRINT TAB(25) "m3";TAB(36) "mol/m3.pa";TAB(52) "kg/m3";LPRINT " "

990 FOR I=1 TO N

995 LPRINT I;TAB(5) COMP\$(I);USING " ###.####";V(I);Z(I);

1000 LPRINT USING " #####.##";D(I)

1005 NEXT I

1010 LPRINT " ";LPRINT " "

1015 IF ZZ=1 THEN GOTO 1050

1020 LPRINT "compartment";TAB(23) "concn";TAB(37) "concn";TAB(50) "amount";TAB(64) "amount";TAB(77) "percent";TAB(92) "reacted"

106) "advected";TA

B(118) "persistence"

1025 LPRINT TAB(22) "mol/m3";TAB(36) "ug/m3";TAB(52) "mol";TAB(67) "kg";TAB(92) "mol/day";TAB(106) "mol/day";TAB(120) "days";LP

" "

1030 FOR I=1 TO N

1035 LPRINT I;TAB(5) COMP\$(I);USING " ###.####";C(I);CM(I);A(I);AK6(I);P(I);RV(I,4);GCO(I);Z(I)

1040 NEXT I

1045 GOTO 1080

1050 LPRINT "compartment";TAB(23) "concn";TAB(37) "concn";TAB(50) "amount";TAB(64) "amount";TAB(77) "percent";TAB(92) "advected"

1055 LPRINT TAB(22) "mol/m3";TAB(36) "ug/m3";TAB(52) "mol";TAB(66) "kg";TAB(92) "mol/day";LPRINT " "

1060 FOR I=1 TO N

1065 LPRINT I;TAB(5) COMP\$(I);USING " ###.####";C(I);CM(I);A(I);AK6(I);P(I);GCO(I)

```

1075 IF ZZ=1 THEN GOTO 1110
1080 LPRINT " ":LPRINT "      Total";TAB(47)
1085 LPRINT USING "##.###^" ";AT;
1090 LPRINT USING "  ##.###^" ";ATK6;
1095 LPRINT USING "   ###.## " ";PT;
1100 LPRINT USING "  ##.###^" ";RTVT;GCOT
1105 GOTO 1135
1110 LPRINT " ":LPRINT "      Total";TAB(47)
1115 LPRINT USING "##.###^" ";AT;
1120 LPRINT USING "  ##.###^" ";ATK6;
1125 LPRINT USING "   ###.## " ";PT;
1130 LPRINT USING "  ##.###^" ";GCOT
1135 LPRINT " "
1140 LPRINT "      fugacity          ";USING "N.###^" Pa";F:LPRINT " "
1145 LPRINT "compartment";TAB(25) "advective flow rate";TAB(50) "advective residence time"
1150 LPRINT TAB(34) "m3/day";TAB(60) "days":LPRINT " "
1155 FOR I=1 TO 2
1160 LPRINT I;TAB(5) COMP$(I);USING "  ##.###^" ";G(I);RES(I)
1165 NEXT I
1170 LPRINT " ":LPRINT "      overall persistence          ";USING "0.###^" days";T
1175 LPRINT "      flow and reaction time          ";USING "0.###^" days";TR
1180 END

```

5 Phase 3 fugacity model

10 DIM V(10),Z(10),D(10),C(10),CH(10),PPM(10),P(10),A(10),ORB(10),ATP(10),ATO(10),CMD(10)

15 DIM COMP\$(10),MAT\$(7)

20 DIM R(10,5),RT(10),RV(10,5),RTV(10),RK(10,5),RKT(10),RP(10,5),RPT(10)

25 DIM G(10),CB(10),GCB(10),GCD(10),GZ(10)

30 DIM ZVK(10),SUMD(10),TK(10,10),TKD(10,10),FDIJ(10,10),FDIJT(10)

35 DIM E(10),F(10),DIJ(10,10),FZVK(10),GC(10),AR(10,10),RES(10,10),TAU(10,10)

40 DIM REST(10),DN(10),DD(10),B(10,10),DE(10,10),Y(10,10),P,QR

45 DEFINT I-J:A\$=" " :B\$=" "

50 N=6

55 'definition of compartment number

60 '1-air,2-water,3-soil,4-sediment

65 '5-suspended aquatic material,6-biota

70 'rk(i,j) refers to rate constant (day-1) in compartment i of process j

75 'j=1 photolysis

80 'j=2 oxidation

85 'j=3 hydrolysis

90 'j=4 biodegradation

95 'j=5 other reactions

100 KEY OFF

105 CLS

110 PRINT "LEVEL 3 FUGACITY CALCULATION"

115 PRINT "An interactive model using microsoft BASIC language.":PRINT " "

120 PRINT "NOTES":PRINT " "

125 PRINT "When using this model, it is immaterial whether values are entered"

130 PRINT "in exponential or non-exponential form,i.e. 2e04 or 20000":PRINT " "

135 PRINT "The results will be printed out on a printer, not on the screen"

140 PRINT "The print width required is 150 characters":PRINT " "

145 PRINT "If you enter an erroneous value, you must start again":PRINT " "

150 PRINT "The parameters required are:

155 PRINT "temperature (deg C)"

160 PRINT "molecular weight (g/mol),vapor pressure (Pa), solubility (g/m3),log Kow

165 PRINT "reaction rate constants (day-1),advective flow rates (m3/day)"

170 PRINT "background or inflow concentrations (mol/m3)":PRINT " "

175 PRINT "We define the six compartments by numbers as follows"

180 PRINT "1-air,2-water,3-soil,4-bottom sediment"

185 PRINT "5-suspended aquatic matter,6-biota":PRINT " "

190 INPUT "press enter to continue";AZ\$

195 CLS

200 PRINT "Note that compartment numbers are:"

205 PRINT "1-air,2-water,3-soil,4-bottom sediment"

210 PRINT "5-suspended aquatic matter,6-biota":PRINT " "

215 INPUT "Do you wish to use the program illustratively (y/n)?":XY\$

220 ET=0

225 IF XY\$="n" THEN GOTO 245

230 E(1)=5:E(2)=50:E(3)=50!:E(4)=0:E(5)=0:E(6)=0

235 FOR I=1 TO N:ET=ET+E(I):NEXT I

240 GOTO 255

245 PRINT "please input emissions into each compartment as 6 numbers one at a time pressing enter after each number. Units are g/day and zero is acceptable"

250 FOR I=1 TO N:INPUT E(I):ET=ET+E(I):NEXT I

255 FOR I=1 TO N:READ COMP\$(I):NEXT I

260 IF XY\$="n" THEN GOTO 265

265 DATA "air", "water", "soil", "sediment", "susp aquat mat", "biota"

270 FOR I=1 TO 6:READ MAT\$(I):NEXT I

275 DATA rate constant matrix (day-1),specific reaction rate (mol/m3day),total reaction rate (mol/day)

```

280 DATA transformation (percent),mass balance (1 day),infinity
285 IF XY$="y" THEN GOTO 340
290 INPUT "What is the compound's name";COMP$(7);PRINT " "
295 PRINT "please input the chemical's physical-chemical properties";PRINT " "
300 INPUT "environmental temperature (deg C), eg. 25";TC
305 INPUT "molecular weight (g/mol), eg. 100 g/mol";WM
310 INPUT "vapour pressure in Pa, eg. 10. (note vap press (Pa)=vap press (atm)x101325 or vap press (pa)=vap press (mm Hg)x13.3)";VPP
315 INPUT "aqueous solubility in g/m3 or equivalent mg/L";SG
320 INPUT "log octanol-water partition coeff Kow, eg. 3.5 (note that it is the log that is requested)";PKOWL
325 INPUT "press enter to continue";ZA$
330 CLS
335 GOTO 370
340 TC=25!
345 COMP$(7)="Hypothetical Compound"
350 WM=350!
355 VPP=.005
360 SG=.035
365 PKOWL=6!
370 RG=8.314
375 'calculate properties
380 TKE=273.15+TC
385 RTT=RG*TKE
390 VPA=VPP/101325!;VPM=VPA*760
395 SM=SG/WM
400 H=VPP/SM;HD=H/RTT
405 PKOW=10!^PKOWL
410 'define areas and volumes
415 AREN=2E+11;AFW=.4;AFS=1-AFW
420 AR(1,2)=AFW*AREA;AR(1,3)=AFS*AREA;AR(2,4)=AFW*AREA
425 FOR I=1 TO N:FOR J=1 TO N:AR(J,I)=AR(I,J):NEXT J:NEXT I
430 V(1)=AREA*2000!;V(2)=AR(1,2)*50;V(3)=AR(1,3)*.15
435 V(4)=AR(2,4)*.03;V(5)=V(2)*5!*.000001;V(6)=V(2)*1!*.000001
440 'define densities
445 D(1)=.029*101325!/RTT
450 D(2)=1000:D(3)=1500:D(4)=1500:D(5)=1500:D(6)=1000
455 'define organic content
460 ORG(3)=.02;ORG(4)=.04;ORG(5)=.04
465 'define partition coefficients
470 PKOC=PKOW*.411
475 PK32=PKOC*ORG(3)
480 PK42=PKOC*ORG(4)
485 PK52=PKOC*ORG(5)
490 PK62=.048*PKOW
495 'define dimensionless partition coefficients
500 PD32=PK32*D(3)/1000
505 PD42=PK42*D(4)/1000
510 PD52=PK52*D(5)/1000
515 PD62=PK62*D(6)/1000
520 'define fugacity capacities
525 Z(1)=1!/RTT
530 Z(2)=1!/H
535 Z(3)=PD32*Z(2)
540 Z(4)=PD42*Z(2)
545 Z(5)=PD52*Z(2)
550 Z(6)=PD62*Z(2)

```

555 CLS

560 IF XY\$="y" THEN GOTO 575

565 PRINT "now we need the reaction rate constants in units of reciprocal days. There are 6 compartments and 5 possible reactions
us there is a poss

ible total of 30 input values. However, in most cases there are only a few reactions."

570 IF XY\$="n" THEN GOTO 620

575 'read in illustrative reaction rate constants (day-1)

580 FOR K=1 TO 4

585 READ I,J,ZK:RK(I,J)=ZK:NEXT K

590 DATA 2,4,3.6e-04,3,4,3.6e-04,4,4,3.6e-03,6,4,2.4e-05

595 'read in illustrative advective inflow (m3/day) and background concentration (mol/m3)

600 FOR K=1 TO 2

605 READ I,GK,CBK:G(I)=GK:CB(I)=CBK:NEXT K

610 DATA 1,2.0e13,0,2,8.0e09,0

615 GOTO 635

620 PRINT "If you do not input a value it will be taken as zero":PRINT " "

625 PRINT "reaction rate constants are entered in the following sequence:- compartment no., reaction no., rate constant (day-1),
separated by commas (

eg. 1,1,.02)":PRINT " "

630 'set rate constants for transfer to stratosphere and sediment burial (day-1) and calculate half-life (years)

635 RK(1,5)=.000041:TAUSTRAT=.693/(RK(1,5)*365)

640 RK(4,5)=.00011:TAUBUR=.693/(RK(4,5)*365)

645 IF XY\$="y" THEN GOTO 780

650 PRINT "note that sediment burial and transfer to the stratosphere are automatically included as other reactions unless you
override them with ze

ro or another value"

655 PRINT "These rate constants are included as:"

660 PRINT "transfer to the stratosphere (1,5,4.1e-05)"

665 PRINT "removal by sediment burial (4,5,1.1e-04)":PRINT " "

670 PRINT "No.:" "Compartment","No.:" "Reaction"

675 PRINT "1:" "Air","1:" "Photolysis"

680 PRINT "2:" "Water","2:" "Oxidation"

685 PRINT "3:" "Soil","3:" "Hydrolysis"

690 PRINT "4:" "Sediment","4:" "Biodegradation"

695 PRINT "5:" "Susp Sediment","5:" "Other"

700 PRINT "6:" "Biota":PRINT " "

705 INPUT "do you want to enter a (or another) rate constant? y/n":XY\$

710 IF XY\$="n" THEN GOTO 720

715 INPUT I,J,ZK:RK(I,J)=ZK:GOTO 705

720 CLS

725 PRINT "Now we require advection rates (m3/day) and the corresponding inflow concentrations (mol/m3)"

730 PRINT "Normally only air and water advection are included, and the background concentrations are zero. If no values are en
tered, zero will be ass
umed.":PRINT " "

735 PRINT "The same procedure is followed as for reaction rate constants except that the requested numbers are: compartment
advective flow rate

(m3/day) and input concentration separated by commas.":PRINT " "

740 PRINT "REMINDER"

745 PRINT "air-1,water-2,soil-3,sediment -4,suspended sediment-5,biota-6":PRINT " "

750 PRINT "a specimen input for Southern Ontario is 1,2.0e13,0 for air advection with zero concentration":PRINT " "

755 PRINT "note that the compartment's residence time is the volume (m3) divided by the flow rate (m3/day), eg. to obtain a
day air residence t

ime, input 1,2.0e13,0"

760 INPUT "do you want to enter a (or another) advective flow rate? y/n":YY\$

765 IF YY\$="n" THEN GOTO 775

770 INPUT I,GK,CBK:G(I)=GK:CB(I)=CBK:GOTO 760

775 PRINT " "

```

780 'calculate overall mass transfer coefficients (tko) and D values
785 'calculate overall mass transfer coefficients tko (m/h) and D values
790 'calculate D value for air-water transfer
795 TK(1,2)=120:TK(2,1)=1.2
800 TKO(1,2)=1/(1!/(TK(1,2)*Z(1))+1!/(TK(2,1)*Z(2)))
805 TKO(2,1)=TKO(1,2)
810 DIJ(1,2)=TKO(1,2)*AR(1,2)
815 DIJ(2,1)=DIJ(1,2)
820 'calculate individual resistances and half-times for transfer
825 RES(1,2)=1/(AR(1,2)*TK(1,2)*Z(1))
830 RES(2,1)=1/(AR(2,1)*TK(2,1)*Z(2))
835 TAU(1,2)=.693/(DIJ(1,2)*(1!/(V(1)*Z(1))+1!/(V(2)*Z(2))))
840 TAU(2,1)=TAU(1,2)
845 'calculate D values for air-soil transfer
850 'for air phase resistance
855 TK(1,3)=240
860 'for soil phase resistance
865 'set air molecular diffusivity (m2/day), mean diffusion depth (m) and air volume fraction in soil
870 DMA=.96:Y3=.075:PHI3=.5
875 'calculate effective diffusivity in soil air
880 DEA=DMA*PHI3^1.5
885 TK(3,1)=DEA/Y3
890 TKO(1,3)=1!/(1!/(TK(1,3)*Z(1))+1!/(TK(3,1)*Z(1)))
895 TKO(3,1)=TKO(1,3)
900 DIJ(1,3)=TKO(1,3)*AR(1,3)
905 DIJ(3,1)=DIJ(1,3)
910 RES(1,3)=1/(AR(1,3)*TK(1,3)*Z(1))
915 RES(3,1)=1/(AR(3,1)*TK(3,1)*Z(3))
920 TAU(1,3)=.693/(DIJ(1,3)*(1!/(V(1)*Z(1))+1!/(V(3)*Z(3))))
925 TAU(3,1)=TAU(1,3)
930 'calculate D values for water-sediment transfer
935 'for water phase resistance
940 TK(2,4)=.24
945 'for sediment phase resistance
950 'set water molecular diffusivity (m2/day), mean diffusion depth (m) and water volume fraction in sediment
955 DMW=9.600001E-05:Y4=.015:PHI4=.5
960 'calculate effective diffusivity in sediment pore water
965 DEW=DMW*PHI4^1.5
970 TK(4,2)=DEW/Y4
975 TKO(2,4)=1!/(1!/(TK(2,4)*Z(2))+1!/(TK(4,2)*Z(2)))
980 TKO(4,2)=TKO(2,4)
985 DIJ(2,4)=TKO(2,4)*AR(2,4)
990 DIJ(4,2)=DIJ(2,4)
995 RES(2,4)=1/(AR(2,4)*TK(2,4)*Z(2))
1000 RES(4,2)=1/(AR(4,2)*TK(4,2)*Z(4))
1005 TAU(2,4)=.693/(DIJ(2,4)*(1!/(V(2)*Z(2))+1!/(V(4)*Z(4))))
1010 TAU(4,2)=TAU(2,4)
1015 'calculate D values for material transfer from soil to water, including water runoff and soil loss
1020 'calculate D for water runoff
1025 WVEL=.28 'velocity of water runoff (m/y)
1030 GWr=WVEL*AR(1,3)
1035 GW=GWr/1365
1040 DIJW32=GW*Z(2)
1045 TAUW32=.693/(DIJW32/(V(3)*Z(3)))

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```

1050 'calculate D for soil loss to water
1055 GSLY=840 'rate of soil loss to water (m3/y)
1060 SVEL=GSLY/AR(1,3)
1065 GSL=GSLY/(365)
1070 DIJS32=GSL*Z(3)
1075 TAU32=.693/(DIJS32/(V(3)*Z(3)))
1080 'calculate total D soil to water
1085 DIJ(3,2)=DIJW32+DIJS32
1090 DIJ(2,3)=0
1095 TAU(3,2)=.693/(DIJ(3,2)/(V(3)*Z(3)))
1100 'calculate D value for water-suspended sediment transfer
1105 'set diffusion half-time (day)
1110 TSS=.042
1115 DIJ(2,5)=V(5)*Z(5)*.693/TSS
1120 DIJ(5,2)=DIJ(2,5)
1125 TAU(2,5)=TSS;TAU(5,2)=TAU(2,5)
1130 'calculate D for material transfer from suspended sediment to sediment
1135 'set suspended sediment deposition rate (m/y)
1140 RD=.0012
1145 GSSY=RD*AR(2,4)
1150 GSS=GSSY/(365)
1155 DIJ(5,4)=GSS*Z(5)
1160 DIJ(4,5)=0
1165 TAU(5,4)=.693/(DIJ(5,4)/(V(5)*Z(5)))
1170 'calculate D value for water-biota transfer
1175 IF XY$="y" THEN ZZ=1
1180 IF XY$="y" THEN GOTO 1205
1185 'calculate D for water-biota transfer
1190 'calculate k2 for biota uptake rate by 1 of 3 methods
1195 'define parameters for uptake correlation
1200 INPUT "for biota-water transfer coefficient use default calculation (1), half-life for uptake (days) (2), or rate constant
-1) (3), indicate
one. When using the program illustratively enter 1";ZZ
1205 TOF=4.2;TMF=.000042
1210 ON ZZ GOTO 1240,1215,1230
1215 INPUT "half-life (days)";THALF
1220 K2=.693/THALF
1225 GOTO 1245
1230 INPUT "rate constant (day-1)";K2
1235 GOTO 1245
1240 K2=1/(TOF+PKOW*TMF)
1245 DIJ(2,6)=V(6)*Z(6)*K2
1250 TAU(2,6)=.693/K2
1255 DIJ(6,2)=DIJ(2,6)
1260 TAU(6,2)=TAU(2,6)
1265 'calculate residence times of phases due to advection
1270 FOR I=1 TO N
1275 ON SGN(G(I))+2 GOTO 1280,1280,1285
1280 REST(I)=0:GOTO 1290
1285 REST(I)=V(I)/G(I)
1290 NEXT I
1295 CLS

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1300 INPUT "Thank you. That is all the information that is required. Do you want the calculation to proceed and print out the res
ts? (y/n)";ZZ$
1305 IF ZZ$="n" THEN GOTO 2665 ELSE GOTO 1310
1310 PRINT " ":PRINT "Please wait . . . ."
1315 FOR I=1 TO N:FOR J=1 TO N
1320 IF I=2 THEN IF J=5 GOTO 1350 ELSE GOTO 1325
1325 IF I=5 THEN IF J=2 GOTO 1350 ELSE GOTO 1330
1330 IF I=2 THEN IF J=6 GOTO 1350 ELSE GOTO 1335
1335 IF I=6 THEN IF J=2 GOTO 1350 ELSE GOTO 1340
1340 IF DIJ(I,J)=0 THEN GOTO 1350
1345 TAU(I,J)=.693/(DIJ(I,J)*(1!/(V(I)*Z(I))+1!/(V(J)*Z(J))))
1350 NEXT J:NEXT I
1355 TAU(2,5)=TSS:TAU(5,2)=TAU(2,5)
1360 TAU(3,2)=.693/(DIJ(3,2)/(V(3)*Z(3)))
1365 TAU(5,4)=.693/(DIJ(5,4)/(V(5)*Z(5)))
1370 TAUW32=.693/(DIJW32/(V(3)*Z(3)))
1375 TAUS32=.693/(DIJS32/(V(3)*Z(3)))
1380 FOR I=1 TO N:FOR J=1 TO 5
1385 RKT(I)=RKT(I)+RK(I,J)
1390 NEXT J
1395 ZVK(I)=Z(I)*V(I)*RKT(I)
1400 GZ(I)=G(I)*Z(I)
1405 GZT=GZT+GZ(I)
1410 GCB(I)=G(I)*CB(I)
1415 GCBT=GCBT+GCB(I)
1420 ET(I)=E(I)+GCB(I)
1425 EGIN=EGIN+ET(I)
1430 NEXT I
1435 EGINK=EGIN*WM/1000
1440 'solve set of n equations of the form aa*f=et
1445 'assemble matrix coefficients
1450 'sum d(i,j) over all j except i
1455 FOR I=1 TO N
1460 SUMD1=0
1465 'set non-diagonal elements
1470 FOR J=1 TO N
1475 IF J=I THEN GOTO 1490
1480 SUMD1=SUMD1+DIJ(I,J)
1485 AA(I,J)=-DIJ(J,I)
1490 NEXT J
1495 SUMD(I)=SUMD1
1500 'set diagonal elements
1505 AA(I,I)=V(I)*Z(I)*RKT(I)+GZ(I)+SUMD(I)
1510 ON SGN(AA(I,I))+2 GOTO 1515,1515,1520
1515 AA(I,I)=.0001
1520 NEXT I
1525 GOSUB 2675
1530 FOR I=1 TO N
1535 C(I)=Z(I)*F(I)
1540 A(I)=C(I)*V(I)
1545 ATP(I)=A(I)*WM/1000000!
1550 AT=AT+A(I)
1555 ATP=AT*WM/1000000!
1560 GCO(I)=G(I)*C(I)
1565 GCDT=GCDT+GCO(I)
1570 PT(I)=0
1575 FOR J=1 TO 5

```

```

1580 R(I,J)=C(I)*RK(I,J)
1585 RV(I,J)=R(I,J)*V(I)
1590 RT(I)=RT(I)+R(I,J)
1595 NEXT J
1600 RTV(I)=RT(I)*V(I)
1605 RTVT=RTVT+RTV(I)
1610 NEXT I
1615 ATK6=AT*WM/1000
1620 FOR I=1 TO N
1625 P(I)=100*A(I)/AT
1630 PT=PT+P(I)
1635 PPM(I)=C(I)*WM*1000/D(I)
1640 CM(I)=C(I)*WM*1000000!
1645 RPT(I)=100*RTV(I)/RTVT
1650 FOR J=1 TO 5
1655 RP(I,J)=100*RV(I,J)/RTVT
1660 NEXT J:NEXT I
1665 RGOT=RTVT+GCOT
1670 RGOTK=RGOT*WM/1000
1675 'calculate residence time and persistence
1680 TR=AT/ESIN:TP=AT/RTVT
1685 FOR I=1 TO N
1690 FZVK(I)=F(I)*ZVK(I)
1695 FOR J=1 TO N
1700 FDIJ(I,J)=DIJ(I,J)*F(I)-DIJ(J,I)*F(J)
1705 FDIJT(I)=FDIJT(I)+FDIJ(I,J)
1710 NEXT J:NEXT I
1715 FDIJWS2=DIJWS2+F(3)
1720 FDIJS32=DIJS32+F(3)
1725 'read in observed concentrations (microg/m3)
1730 FOR I=1 TO N:READ CM0(I):NEXT I
1735 DATA 5e-03,9,1e04,1e05,0,1e06
1740 WIDTH "lpt1:",150
1745 LPRINT CHR$(15)
1750 LPRINT "date: ";DATE$;"time: ";TIME$:LPRINT " "
1755 LPRINT "Phase 3 calculation":LPRINT " "
1760 LPRINT COMP$(7):LPRINT " ":LPRINT "compound properties":LPRINT " "
1765 LPRINT "molecular weight";A$:A$:USING "#####.## g/mol":WM
1770 LPRINT "aqueous solubility";A$:A$:USING "###.##### g/m3":SB:
1775 LPRINT USING " or ###.##### mol/m3":SM
1780 LPRINT "vapour pressure";A$:A$:USING "###.##### pa":VPP:
1785 LPRINT USING " or ###.##### atm":VPA:
1790 LPRINT USING " or ###.##### mm Hg":VPM
1795 LPRINT "henry's constant";A$:A$:USING "###.##### pa m3/mol":H
1800 LPRINT "octanol-water part coeff (log)":B$:B$:USING "#####.##":PKOWL:
1805 LPRINT USING " part coeff ###.##":PKOM
1810 LPRINT "temperature";A$:A$:B$:USING "#####.## deg C":TC:
1815 LPRINT USING " or #####.## K":TKE
1820 LPRINT " "
1825 LPRINT "compartment";TAB(25) "volume";TAB(41) "z":
1830 LPRINT TAB(53) "density";TAB(68) "amount":
1835 LPRINT TAB(80) "percent";TAB(105) "concentrations"
1840 LPRINT TAB(28) "m3":TAB(38) "mol/m3.pa":
1845 LPRINT TAB(54) "kg/m3":TAB(69) "mol":TAB(92) "mol/m3":TAB(107) "microg/g":
1850 LPRINT TAB(122) "microg/m3":LPRINT " "
1855 FOR I=1 TO 6

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1860 LPRINT I;TAB(5) COMP$(I);USING " ##.####^";V(I);Z(I);
1865 LPRINT USING " #####.##";D(I);
1870 LPRINT USING " ##.####^";A(I);
1875 LPRINT USING " ###.## ";P(I);
1880 LPRINT USING " ##.#####^";C(I);PPM(I);CM(I)
1885 NEXT I
1890 LPRINT " "
1895 LPRINT " Total";TAB(65);
1900 LPRINT USING "##.####^ ";AT;
1905 LPRINT USING " ###.##";PT
1910 LPRINT TAB(62);USING "or ##.####^ kg";ATKG
1915 LPRINT " "
1920 LPRINT "flow and reaction time";USING " #####.## days";TR;
1925 LPRINT " reaction persistence";USING " #####.## days";TP
1930 LPRINT " ":LPRINT " ":LPRINT " "
1935 LPRINT "summary of compartment mass balances (mol/day)":LPRINT " "
1940 LPRINT TAB(19) "emissions";TAB(38) "inflow";TAB(55) "reaction";TAB(73) "outflow";
1945 LPRINT TAB(91) "transport";TAB(109) "fugacity (pa)":LPRINT " "
1950 FOR I=1 TO N
1955 LPRINT COMP$(I);
1960 LPRINT USING " ##.#####^ ";E(I);GCB(I);FZVK(I);GCO(I);FDIJT(I);F(I)
1965 NEXT I
1970 LPRINT " ":LPRINT "Total";TAB(16);
1975 LPRINT USING " ##.#####^ ";ET;GCBT;RTVT;GCOT;LPRINT " ":LPRINT " "
1980 LPRINT "total input (emissions and inflow)":TAB(40);
1985 LPRINT USING " ##.####^ mol/day";EGIN;
1990 LPRINT USING " ##.####^ kg/day";EGINK
1995 LPRINT "total output (reactions and outflow)":TAB(40);
2000 LPRINT USING " ##.####^ mol/day";RGT;
2005 LPRINT USING " ##.####^ kg/day";RGTK
2010 LPRINT CHR$(12)
2015 MI=1
2020 LPRINT " ":LPRINT MAT$(MI);LPRINT " ":LPRINT "compartment";TAB(26) "photolysis";
2025 LPRINT TAB(45) "oxidation";TAB(64) "hydrolysis";TAB(83) "biodegradation";
2030 LPRINT TAB(102) "other";TAB(116) "total":LPRINT " "
2035 ON MI GOTO 2040,2065,2090,2115
2040 FOR I=1 TO 6
2045 LPRINT COMP$(I);B$;
2050 FOR J=1 TO 5:LPRINT B$;USING "##.####^";RK(I,J);:NEXT J
2055 LPRINT USING "##.#####^ ";PKT(I);:NEXT I
2060 MI=2:GOTO 2020
2065 FOR I=1 TO 6
2070 LPRINT COMP$(I);B$;
2075 FOR J=1 TO 5:LPRINT B$;USING "##.#####^ ";R(I,J);:NEXT J
2080 LPRINT USING "##.#####^";RT(I);:NEXT I
2085 MI=3:GOTO 2020
2090 FOR I=1 TO N
2095 LPRINT COMP$(I);B$;
2100 FOR J=1 TO 5:LPRINT B$;USING "##.#####^ ";RV(I,J);:NEXT J
2105 LPRINT USING "##.#####^";RTV(I);:NEXT I
2110 MI=4:GOTO 2020

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2115 FOR I=1 TO 6
2120 LPRINT COMP$(I);
2125 FOR J=1 TO 5:LPRINT B$;B$;USING "##.#####";RP(I,J);NEXT J
2130 LPRINT B$;USING "##.#####";RPT(I);NEXT I
2135 LPRINT " ":LPRINT MAT$(5):LPRINT " "
2140 LPRINT TAB(27) "inflows";TAB(48) "outflows";TAB(69) "flow m3/day";
2145 LPRINT TAB(87) "inflow conc mol/m3";TAB(109) "residence time day":LPRINT " "
2150 FOR I=1 TO 6
2155 ON SGN (REST(I)-0)+2 GOTO 2160,2160,2175
2160 LPRINT COMP$(I);B$;B$;USING "##.#####";GCB(I);GCD(I);G(I);CB(I);
2165 LPRINT MAT$(6)
2170 GOTO 2180
2175 LPRINT COMP$(I);B$;B$;USING "##.#####";GCB(I);GCD(I);G(I);CB(I);REST(I)
2180 NEXT I
2185 LPRINT " "
2190 LPRINT USING " other rate constant from air of 4.1e-05 represents transfer to stratosphere half-time ##.###";TAUSTR=
2195 LPRINT " year"
2200 LPRINT USING " other rate constant from sediment of 1.1e-04 represents burial half-time ##.###";TAUBUR=
2205 LPRINT " year":LPRINT " "
2210 LPRINT CHR$(12)
2215 LPRINT "transfer rate coefficients between compartments"
2220 LPRINT " ":LPRINT "No.":B$;"compartment":LPRINT " "
2225 FOR I=1 TO 6
2230 LPRINT I;TAB(9) COMP$(I)
2235 NEXT I
2240 LPRINT " ":LPRINT TAB(6) "compartment ";TAB(27) "D";TAB(33) "transport rate";TAB(49) "interfacial";TAB(64) "k(i,j)";TAB(77)
I,I":TAB(89) "k o
verall";
2245 LPRINT TAB(101) "res(i,j)";TAB(112) "res(j,i)";TAB(124) "tau(i,j)"
2250 LPRINT A$;B$;"(mol/day*pa)";" (mol/day)";" area (m**2)";B$;"(m/day)";B$;" (m/day)";A$;A$;B$;B$;"(day)":LPRINT " "
2255 J=2
2260 FOR I=1 TO 2
2265 IF DIJ(I,J)=0 THEN GOTO 2300
2270 LPRINT USING "from ##";I;
2275 LPRINT USING " to ## ";J;
2280 LPRINT USING " ##.#####";DIJ(I,J);FDIJ(I,J);AR(I,J);TK(I,J);TK(J,I);TKO(I,J);
2285 LPRINT USING " ##.#####";RES(I,J);RES(J,I);
2290 LPRINT USING " #####.##";TAU(I,J)
2295 J=J-1
2300 NEXT I
2305 LPRINT " ":LPRINT " "
2310 J=3
2315 FOR I=1 TO 3 STEP 2
2320 LPRINT USING "from ##";I;
2325 LPRINT USING " to ## ";J;
2330 LPRINT USING " ##.#####";DIJ(I,J);FDIJ(I,J);AR(I,J);TK(I,J);TK(J,I);TKO(I,J);
2335 LPRINT USING " ##.#####";RES(I,J);RES(J,I);
2340 LPRINT USING " #####.##";TAU(I,J)
2345 J=J-2
2350 NEXT I
2355 LPRINT " "
2360 J=4
2365 FOR I=2 TO 4 STEP 2
2370 LPRINT USING "from ##";I;

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2375 LPRINT USING " to ## ";J;
2380 LPRINT USING " ##.####";DIJ(1,J);FDIJ(1,J);AR(1,J);TK(1,J);TK(J,1);TKO(1,J);
2385 LPRINT USING " ##.####";RES(1,J);RES(J,1);
2390 LPRINT USING " #####.##";TAU(1,J)
2395 J=J-2
2400 NEXT I
2405 LPRINT " ":LPRINT TAB(6) "compartment";TAB(26) "D";TAB(33) "transport rate";TAB(50) "tau(i,j)"
2410 LPRINT A$;B$; " (mol/day*pa)";B$; "(mol/day)";LPRINT " "
2415 J=5
2420 FOR I=2 TO 5 STEP 3
2425 LPRINT USING "from ##";I;
2430 LPRINT USING " to ## ";J;
2435 LPRINT USING " ##.####";DIJ(1,J);FDIJ(1,J);
2440 LPRINT USING " #####.##";TAU(1,J)
2445 J=J-3
2450 NEXT I
2455 LPRINT " ":LPRINT TAB(6) "compartment";TAB(26) "D";TAB(33) "transport rate";TAB(53) "k2";TAB(64) "tau(i,j)"
2460 LPRINT TAB(22) "(mol/day*pa)";TAB(36) "(mol/day)";TAB(50) "(day-1)";TAB(65) "(day)";LPRINT " "
2465 J=6
2470 FOR I=2 TO 6 STEP 4
2475 LPRINT USING "from ##";I;
2480 LPRINT USING " to ## ";J;
2485 LPRINT USING " ##.####";DIJ(1,J);FDIJ(1,J);K2;
2490 LPRINT USING " #####.##";TAU(1,J)
2495 J=J-4
2500 NEXT I
2505 LPRINT " ":LPRINT TAB(6) "compartments";TAB(23) "by";TAB(42) "D";TAB(50) "transport rate";TAB(66) "flow";TAB(79) "flow";
"tau(i,j)";TAB(11
5) "velocity"
2510 LPRINT TAB(38) "(mol/day*pa)";TAB(53) "(mol/day)";TAB(65) "(m3/day)";TAB(79) "(m3/y)";TAB(97) "(day)";TAB(117) "(m/y)";L
"
2515 LPRINT "from 3";
2520 LPRINT " to 2 water";TAB(33);
2525 LPRINT USING " ##.####";DIJW32;FDIJW32;GW;GWR;
2530 LPRINT USING " ##.####";TAUW32;WVEL
2535 LPRINT "from 3";
2540 LPRINT " to 2 soil ";TAB(33);
2545 LPRINT USING " ##.####";DIJS32;FDIJS32;GSL;GSLY;
2550 LPRINT USING " ##.####";TAUS32;SVEL
2555 LPRINT "from 3";
2560 LPRINT " to 2 total";TAB(33);
2565 LPRINT USING " ##.####";DIJ(3,2);FDIJ(3,2);
2570 LPRINT TAB(92) USING " #####.##";TAU(3,2);LPRINT " "
2575 LPRINT "from 5";
2580 LPRINT " to 4 ";TAB(33)
2585 LPRINT USING " ##.####";DIJ(5,4);FDIJ(5,4);GSS;GSSY;
2590 LPRINT USING " #####.##";TAU(5,4);LPRINT " ":LPRINT " "
2595 LPRINT USING "air molecular diffusivity ##.####";DMA;
2600 LPRINT "m2/day";
2605 LPRINT USING " air effective diffusivity ##.####";DEA;
2610 LPRINT "m2/day ";
2615 LPRINT USING " porosity ##.##";PHI3;
2620 LPRINT USING " mean path length ##.## ";L3;
2625 LPRINT " "

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2630 LPRINT USING "water molecular diffusivity %.##^#### ";DMW;
2635 LPRINT "m2/day";
2640 LPRINT USING " water effective diffusivity %.##^#### ";DEM;
2645 LPRINT "m2/day";
2650 LPRINT USING " porosity %.# ";PHI4;
2655 LPRINT USING " mean path length %.## ";Y4;
2660 LPRINT " "
2665 PRINT " ":PRINT "The End"
2670 END
2675 'subroutine using Gaussian elimination to solve n equations for f(i)
2680 FOR I=1 TO N
2685 DD(I)=ET(I)
2690 FOR J=1 TO N
2695 B(I,J)=AA(I,J)
2700 NEXT J:NEXT I
2705 NQ=N-1
2710 FOR K=1 TO NQ
2715 DEN=1/B(K,K)
2720 DD(K)=DEN*DD(K)
2725 KK=K+1
2730 FOR J=KK TO N
2735 B(K,J)=DEN*B(K,J)
2740 NEXT J
2745 FOR I=KK TO N
2750 DD(I)=DD(I)-DD(K)*B(I,K)
2755 FOR J=KK TO N
2760 B(I,J)=B(I,J)-B(K,J)*B(I,K)
2765 NEXT J:NEXT I:NEXT K
2770 F(N)=DD(N)/B(N,N)
2775 FOR I=1 TO NQ
2780 K=N-I
2785 F(K)=DD(K)
2790 FOR J=1 TO I
2795 L=K+J
2800 F(K)=F(K)-B(K,L)*F(L)
2805 NEXT J:NEXT I
2810 RETURN

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